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Original Articles

A STUDY OF CERTAIN FACTORS INFLUENCING RESULTS OF ARTIFICIAL PNEUMOTHORAX TREATMENT

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A LARGE number of reviews of the results of artificial pneumothorax treatment in general have been published including several dealing with series of Indian patients, e.g. Pai (1927), Frimodt-Möller (1928), Frimodt-Möller and Verghese (1937). No further reports are needed to emphasize the value of the treatment, but

We have analysed the figures according to the type of disease, the extent and localization of the lesion, the presence of cavities, the nature of the collapse, whether selective, partial, or contra-selective, the presence of contralateral lung disease, effusion and other complications. All the classifications have been made from a study of x-ray films.

We originally classified all our observations according to sex and according to whether the artificial pneumothorax was given for the right or left lung, but we found no significant difference either between the sexes or the sides treated, and so for economy of space, these details have been omitted from this paper.

For the main analysis, the 409 patients who received artificial pneumothorax for three months and more are taken. We have grouped patients discharged as 'arrested', 'quiescent', 'much improved', 'improved', all under the heading 'improved'.

Type of disease

If we divide the 409 cases according to the type of disease and the results of treatment, we find the following points (table I).

TABLE I

Type of disease	Number treated	IMPROVED		SPUTUM NEGATIVE	
		Number	Per cent	Number	Per cent
Caseo-pneumonic ..	19	11	57.9	7	36.8
Predominantly exudative ..	244	171	70.1	137	56.1
Mixed ..	109	80	73.4	60	55.1
Predominantly fibrotic ..	37	33	89.2	28	75.7

special investigations are still needed to add to our knowledge of the factors which influence the result of artificial pneumothorax treatment, favourably or otherwise, in individual patients.

Material analysed

For this purpose, out of our series of 3,657 patients in whom artificial pneumothorax has been tried, we have studied certain points in 781, that is, in all patients in whom artificial pneumothorax has been attempted in the period from 1st January, 1940 to 31st December, 1943, and who have completed their treatment in the institution and have been discharged. Of these 781 cases, 81 are excluded because they stayed less than one month. This leaves 700 for detailed analysis.

This group is subdivided as follows: a group of 409 patients who received artificial pneumothorax treatment for three months or more; a group of 277 composed of 100 patients who received artificial pneumothorax for less than three months and 177 in whom artificial pneumothorax was attempted but no free pleural space could be found owing to extensive adhesions; in addition 14 patients are excluded as they had either thoracoplasty or extrapleural pneumothorax subsequent to the artificial pneumothorax on the original pneumothorax side.

In the figures given in table I under 'improved', the only significant difference is in the predominantly fibrotic group; this indicates that artificial pneumothorax treatment is of the same value in caseo-pneumonic, predominantly exudative and mixed types, but the fibrotic group shows a better prognosis.

The same conclusion is arrived at when we study improvement as judged by the disappearance of tubercle bacilli. There is no significant difference between the more exudative types, but the fibrotic type shows a better result of treatment.

The question whether this significance in the fibrotic group could be due to any other essential factor in the group as compared with the other groups investigated; was it due to the small extent of the disease, the absence of cavities, or the absence of contralateral lung disease? These points are studied in table II.

The table shows that there is no essential difference in these three groups, and it may be assumed that the better results in the fibrotic group are due to the fibrotic nature of the disease.

TABLE II

	FIBROTIC (37)		OTHER TYPES (372)	
	Num- ber	Per cent	Num- ber	Per cent
One lung zone only affected	4	10.8	61	16.7
Contralateral lung affected	35	67.6	257	69.1
Cavities present ..	30	81.1	332	89.2

Extent of disease

We have divided the patients according to the number of zones affected in the lung as seen in the x-ray film at the time of beginning artificial pneumothorax treatment (zones are recorded according to the standard recommended by the Tuberculosis Association of India). The zones are given separately and also added together into one, two, or three zones (table III).

Where all the zones are affected, the prognosis is less good than where one or two

zones are affected, a result which we naturally expect. But there is no significant difference between patients with one zone affected and those with two, a result contrary to expectation, except where the upper zone only is affected, when the results are significantly superior to middle- or two-zone affections.

Cavities.—If the patients are divided according to the presence or absence of cavities, we find the following results (table IV).

Judged from improvement, the difference between the patients with a single cavity and those with more than one is not significant, but, as we should expect, those with no cavity have a better result. Judged from the disappearance of tubercle bacilli from the sputum, we find a significant difference between each of the groups, the result being progressively worse with one cavity and more than one cavity.

Nature of collapse

If the figures are analysed according to the nature of the collapse in the artificial pneumothorax side, we find the following results (table V).

TABLE III

Zone	Number treated	IMPROVED		SPUTUM NEGATIVE	
		Number	Per cent	Number	Per cent
Upper only ..	25	22	88.0	20	80.0
Middle only ..	34	25	73.5	19	55.8
Lower only ..	5	3	60.0	2	40.0
Upper and middle	233	179	76.8	141	60.7
Middle and lower	29	21	72.4	19	65.5
Upper and lower	2	1	50.0	1	50.0
All zones ..	81	44	54.3	30	37.3

TABLE IV

Cavities	Number treated	IMPROVED		SPUTUM NEGATIVE	
		Number	Per cent	Number	Per cent
No cavity ..	47	43	91.6	38	80.9
One cavity ..	285	205	71.9	163	57.2
More than one cavity ..	77	47	61.0	31	40.3

TABLE V

Nature of collapse	Number treated	IMPROVED		SPUTUM NEGATIVE	
		Number	Per cent	Number	Per cent
Selective ..	189	149	78.8	118	62.4
Partial ..	211	142	67.3	111	52.6
Contra-selective ..	9	4	44.4	3	33.3

Selective collapse naturally gives better results than partial or contra-selective collapse, but nevertheless 67.3 per cent of patients with a partial collapse showed improvement.

Judging improvement by the disappearance of tubercle bacilli from the sputum, we find the difference between the selective collapse and the others is just significant, and this indicates that the nature of the collapse has some influence on the disappearance of bacilli. We should naturally have expected a greater significance.

If we investigate why 40 or 21.2 per cent of those with a selective collapse failed to show improvement, and 71 or 37.6 per cent failed to get rid of their bacilli, certain points arise. These are summarized in table VI.

TABLE VI
189 patients with selective collapse

Condition	Improved 149		Not improved 40		T.B. negative 118		T.B. positive 72	
	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent
Unilateral disease ..	57	38.3	5	12.5	48	40.7	14	19.8
Bilateral disease ..	92	61.7	35	87.5	70	59.3	57	80.3
Cavities present in contra-lateral lung.	24	16.0	17	42.5	11	9.3	28	39.8
Spontaneous pneumothorax A.P. side.	2	1.3	4	10.0	1	0.85	5	7.0
Spontaneous pneumothorax con-tralateral side.	3	2.0	1	2.5	3	2.5	1	1.4
Contra-lateral extension ..	7	4.7	3	7.5	2	1.70	8	11.3
Intestinal tuberculosis ..	9	6.0	8	20.0	8	6.8	9	12.7
Diabetes ..	10	6.7	7	22.5	8	6.8	11	15.5

We find that the unimproved had a preponderance of adverse factors weighing against them at the time of starting the artificial pneumothorax.

Condition of contralateral lung

In the 409 patients, we find the condition of the contralateral lung as follows, compared with the results (table VII):—

TABLE VII

Condition of contralateral lung	Num-ber of patients	IMPROVED		SPUTUM NEGATIVE	
		Num-ber	Per cent	Num-ber	Per cent
No disease ..	127	115	90.6	104	81.9
Disease ..	282	180	63.8	128	45.4

Again, as would be expected, there is a significant difference between those with no disease in the contralateral lung and those with disease. If we examine in more detail the condition of the contralateral lung in the 282 patients with bilateral disease, we find as follows.

TABLE VIII

Extent of disease in contralateral lung	Num-ber of patients	IMPROVED		SPUTUM NEGATIVE	
		Num-ber	Per cent	Num-ber	Per cent
One zone ..	141	93	66.0	73	51.8
Two zones ..	119	76	63.9	50	42.0
Three zones ..	22	11	50.0	25	22.7

From this it will be seen that 66.0 per cent of those with involvement of one zone in the contra-lateral lung improved as compared with 90.6

per cent with no contralateral disease (table VII), that is, as would be expected, there is a less good prognosis in patients with bilateral affection even with only one zone affected in the contralateral lung. The same applies to the disappearance of bacilli. However, there appears to be no significant difference between those with one and those with two zones affected in the contralateral lung. This corresponds with what was found in the artificial pneumothorax side, namely, that one and two zones have approximately the same prognosis, but the prognosis is definitely worse if all three zones are affected.

Of the 282 patients with bilateral disease, 182 had no special treatment for the contralateral lung, and of these, 125 or 68.7 per cent showed improvement. The remaining 100 had special treatment such as artificial pneumothorax 54, phrenic nerve operation 5, thoracoplasty 7, extrapleural pneumothorax 2, sanocrysin 32. Of these, 55 or 55 per cent, showed an improvement. On investigation, however, we find these two groups are not really comparable, as those for which no special treatment was given for the contralateral lung had less severe disease as judged by the number of zones affected and cavity formation.

Complications of artificial pneumothorax

(a) *Mediastinal displacement.*—Does displacement of the mediastinum influence the result of artificial pneumothorax treatment? This was investigated from the point of view of improvement and of disappearance of tubercle bacilli.

TABLE IX

Mediastinum	Number treated	IMPROVED		SPUTUM NEGATIVE	
		Number	Per cent	Number	Per cent
Displaced ..	147	98	66.7	76	51.8
Not displaced ..	262	197	75.1	156	59.5

There is no significant difference between the two groups. We have found the same absence of significance in the cases with selective collapse taken separately, there being 58 cases with mediastinal displacement in 149 improved selective collapse cases and 17 in 40 unimproved selective collapse cases.

(b) *Effusion.*—Investigation of the effect of pleural effusion on the general results shows that it makes no significant difference.

TABLE X

Effusion in A.P.	Number treated	IMPROVED	
		Number	Per cent
Absent ..	120	93	77.8
Present ..	289	202	69.9

From the point of view of effusion and type of lesion we find as follows.

TABLE XI

Type	Number treated	EFFUSION PRESENT	
		Number	Per cent
Caseo-pneumonic	19	18	94.8
Predominantly exudative.	244	170	69.6
Mixed	109	76	69.7
Predominantly fibrotic.	37	25	67.6

Effusion is much more likely to occur in caseo-pneumonic types, but there is no difference between the other three types.

We have also investigated the time of onset of effusion in relation to the type of lesion, and the nature of the fluid whether clear or turbid, and have found no significant difference between any of the types.

(c) *Intestinal tuberculosis.*—We have found that intestinal tuberculosis seriously affects the results of treatment in artificial pneumothorax. The diagnosis of intestinal tuberculosis was mainly on clinical evidence, as routine barium-meal examination was not made in all cases.

TABLE XII

Intestinal tuberculosis	Number of patients	IMPROVED	
		Number	Per cent
No symptoms noted	364	273	75.0
Diagnosed ..	45	22	48.9

(d) *Spontaneous pneumothorax.*—There is a highly significant difference between patients experiencing rupture of the lung on the artificial pneumothorax side, and those without this complication.

TABLE XIII

Rupture of lung	Number of patients	IMPROVED	
		Number	Per cent
Nil ..	389	289	74.4
Present ..	21	7	33.3

(e) *Diabetes mellitus.*—Diabetes was found in 30 of the pneumothorax treated cases. But it does not seem to be of significance as regards results of treatment.

TABLE XIV

Diabetes	Number of patients	IMPROVED	
		Number	Per cent
Present ..	30	17	56.7
Absent ..	379	278	73.6

Can 'failed' pneumothorax cases be used as controls?

At the beginning of the paper, it was stated that 100 patients had artificial pneumothorax for less than three months, and in 177 no free pleural space could be found. Sometimes this type of patient is used as a control to judge the results of treatment in cases in which pneumothorax has been successfully induced. As a side-line of our main analysis, we have examined whether such cases can be fairly used as controls.

Taking first of all the type of disease: are the successful and failed pneumothorax cases comparable groups?

TABLE XV

Type of disease	A.P. CASES		FAILED A.P. CASES	
	Number	Per cent	Number	Per cent
Caseo-pneumonic	19	4.7	23	8.3
Predominantly exudative.	244	59.6	149	53.8
Fixed	109	26.7	61	22.0
Predominantly fibrotic.	37	9.0	44	15.9
TOTAL ..	409	100.0	277	100.0

In the two large groups, there is not much difference in distribution, but in caseo-pneumonic and fibrotic types, there is an excess in the 'failed' group. That is, taken as a whole, from the point of view of the type, the two groups are not quite comparable.

If, however, we take the largest group—predominantly exudative—in which there is not much difference, and examine further, we find that there are more patients with all zones affected in the failed cases than there are in the successful (table XVI).

TABLE XVI
Predominantly exudative cases

Zones affected	A.P. CASES		FAILED A.P. CASES	
	Number	Per cent	Number	Per cent
One ..	47	19.3	18	12.1
Two ..	144	59.0	83	55.7
Three ..	53	21.7	48	32.2
TOTAL ..	244	100.0	149	100.0

Looking at these findings in another way, we find that there is an increasing number with obliterated pleural space with increasing lung affection (table XVII).

TABLE XVII
Predominantly exudative cases

Zones affected	Total patients	FAILED A.P. CASES	
		Number	Per cent
One ..	65	18	27.7
Two ..	227	83	36.6
Three ..	101	48	47.5

Therefore, separation of cases into successful and failed pneumothorax groups will include in the failed group more cases with a wide extension of the disease.

Further, there are more cases with contralateral lung disease in the failed group than

in the successful group. Taking again the predominantly exudative groups, we find that out of 244 with successful pneumothorax, 163 or 66.8 per cent were bilateral, and of 149 with 'failed' pneumothorax 121 or 81.2 per cent were bilateral. Therefore, in this respect also the two groups are not comparable.

Therefore, at least in the series of cases included in this review, it would not be correct to take as 'controls' for the study of pneumothorax treatment, the cases in which this treatment has not been possible.

Summary and conclusions

(1) Of a consecutive series of 781 patients in whom artificial pneumothorax was attempted 409 had a successful induction and maintenance for more than three months.

(2) The results following artificial pneumothorax treatment in these are analysed according to the type of disease in the patients treated, the extent of lesions, the presence of cavities, the nature of the collapse, the condition of the contralateral lung, and complications including mediastinal displacement, pleural effusion, intestinal tuberculosis, spontaneous pneumothorax and diabetes.

(3) The question of controls is discussed.

(4) (a) It is shown that the patients with a predominantly fibrotic type of disease have better results than those with other types, while these show no significant difference between themselves.

(b) Except for a larger percentage of good results in patients with only upper zone affection, there is no significant difference between one zone and two zone affections; when all the zones are affected, there is a worse prognosis.

(c) Judged by improvement, there does not seem to be much difference between one-cavity cases and multiple-cavity cases, but sputum results are better in the former. Cases with no cavity, as can be expected, show still better results.

(d) Those with a selective collapse show better results, but not as marked as might have been expected.

(e) Cases with contralateral lung involvement show a worse prognosis.

(f) Mediastinal displacement, pleural effusion and diabetes make no significant difference in the results of treatment. Intestinal tuberculosis and spontaneous pneumothorax affect the prognosis adversely.

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CARBOHYDRATE METABOLISM IN THE DIFFERENT PATHOLOGICAL TYPES OF PULMONARY TUBERCULOSIS

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Introduction

STUDIES of tuberculous lungs by means of x-ray plates and histopathological preparations afford an understanding of anatomo-pathological changes produced by the tubercle bacillus, but such studies do not reveal the physio-pathological changes which go along with it, not only in the lungs but in the body as a whole. We are, therefore, concerned in this paper with deviations from the normal or biochemical functions, caused by the settling of the tubercle bacillus in the lung. Structural examinations have given information as to the route within the lungs on which a present re-infection or a re-activation [Pagel (1935), Siegen (1926), Ghon (1926)] has developed from a former 'primary focus'. But why such an endogenous re-infection or re-activation takes place after many years of healthy life, why a primary focus in one person produces immunity, renders another person allergic, and sensitizes (producing anaphylactic shock) a third person (or experimental animal), we are not in a position to investigate with the anatomical and radiological methods at our disposal.

We do not know what biochemical conditions within the body are congenial to the growth and multiplication of the bacilli, resulting in the various different histological changes, viz, exudation, fibrosis, caseation, acinar productive tubercles, or resolution of exudation. If we consider the comparative infrequency of conjugal tuberculosis and tuberculosis in attendants in sanatoriums, it is obvious that the bacillus alone does not account for the disease. Pottenger (1934) for instance reports not one case of infection to attendants in his sanatorium within 30 years; in our sanatorium, only one such case was reported 30 years ago (an alcoholic), and no relapse of any ex-patient member of the medical staff. Some other factor must be responsible for the development of the bacillus and the production of the various phenomena in the lung. Epidemiological data of 1,000 patients, treated in our sanatorium during the last 6 years, reveal only 29 per cent of cases with a history indicating a probable source of infection. Other statistics, taken from the 173 patients at present under treatment in our sanatorium, showed a figure as high as 29.4 per cent for metabolic diseases from which the patients themselves or their near relatives were suffering.

The term 'diminished resistance' generally given as the reason for the development of

pulmonary tuberculosis in an individual, comprises among other factors, diabetes, pregnancy, gestation, lactation, starvation and shock. They all indicate again disorders of a functional character of the metabolism or the endocrine glands. Also the literature furnishes proof that a relation exists, for instance, between pulmonary tuberculosis and the carbohydrate metabolism in particular.

Literature

In the older literature of diabetes, the incidence of tuberculosis was much more frequent than it is now after the introduction of insulin. Curschmann (1928) noted that tuberculosis was present in 42 to 50 per cent of the diabetics. In autopsy-reports of diabetic patients up to the times of Naunyn, an incidence of 42 per cent with active tuberculosis was present (Goldberg, 1939). Since the introduction of insulin, the incidence of tuberculosis has dropped down to between 2.4 and 10 per cent. 'Galloping tuberculosis' in the course of diabetes seen in fore-insulin days is now no more seen (Billimoria, 1940).

The good effect of insulin on the general condition of tuberculous patients is recognized by Allen, Lang and Keeton (Goldberg, 1939). The explanation, however, given for the improvement through insulin, is its fattening property on thin patients with poor appetite. Certain clinicians suggest that insulin is such a powerful metabolic catalyst that the diabetic has a greater chance of recovery from the tuberculosis than his non-diabetic brother. This has, however, not led to the general use of insulin for the treatment of non-diabetic tuberculous patients.

On the other hand, it is an old clinical observation that the diabetes of a person improves when tuberculosis supervenes [Bose (1939), Joslin *et al.* (1940)]. Joslin puts it in the words: 'When the diabetes is doing well and the patient poorly, suspect tuberculosis.' Naunyn ranks tuberculosis in the first place of diseases which ameliorate diabetes. Bose (1939) reports in three cases the disappearance of the diabetic symptoms and also the improvement in the patient's tolerance for carbohydrates after the development of pulmonary tuberculosis. We also have the history of three tuberculous diabetics who observed on themselves an amelioration of their diabetic symptoms, viz, polydipsia and polyuria, after development of their tuberculosis, before insulin treatment. Trying to explain these observations, Lundberg (1925) has advanced an hypothesis; he claims to have found in the tuberculous lung an insulin-like body, called by him para-insulin, which injected into white mice causes hypoglycæmic symptoms. From his clinical observations, Billimoria (1940) is also of the opinion that the caseous type of lesion seems to secrete some insulin-like substance, and the urine and blood sugar often drop markedly. He has

seen these drops even with full diet and he, therefore, does not attribute this phenomenon to anorexia and low diet. On the other hand, Lundberg's experiments and views are contradicted by Curschmann (1928). Other authors such as Allen suggest that the improvement in diabetes in association with tuberculosis is due to undernutrition, and that the improvement in the incidence and the mortality rate of pulmonary tuberculosis among diabetic patients is due chiefly to better control of the diabetes brought about through the use of insulin (Joslin *et al.*, 1940).

We believe that all the above observations and facts, although waiting for a full scientific elucidation, are proof of an existing relationship between tuberculosis and the carbohydrate metabolism. The following experiments were undertaken in order to study this relationship, and to deal with possible functional disturbances of the carbohydrate metabolism in relation to pulmonary tuberculosis.

Method

In our series of 62 sugar-tolerance tests on 50 unselected afebrile tuberculous patients, we used the oral test. We gave 50 gm. glucose in about 100 c.cm. of plain tea in the morning after a fast of about 14 hours and after having taken a blood specimen. We then took blood again from the vein after intervals of 25, 60, 90 and 120 minutes, sometimes still more frequently, as seen in our curves. Immediately afterwards we started the blood-sugar determination with the methods of Hagedorn-Jensen. For each determination we took two blood samples, the difference of which did not as a rule exceed 10 mg. per cent. During the tests the patients were resting; smoking was not permitted. Urine examinations for sugar by Benedict's qualitative methods were carried out during fasting and one and a half hours after the intake of the 50 gm. glucose. Except in our tuberculous diabetic patients, the result of these urine examinations was, as a rule, always negative.

Simultaneously when taking blood for sugar estimations, we reserved about 1 c.cm. of blood for density determinations, which we kept separately in centrifuge tubes tightly stoppered. Such density determinations were carried out at the same intervals as the blood-sugar determinations. These determinations of the specific gravity were carried out in the serum on the same day with La Motte's falling drop densimeter, employing the Barbour and Hamilton method (1926).

Results

Before evaluating the results of sugar-tolerance tests without taking into consideration the kind of treatment, we had to determine whether pneumothorax treatment and injections of gold and calcium, by themselves, had any influence on the tests. Figure 1 showing graphically on the same patient the results of the oral glucose-tolerance test before and one month after the artificial pneumothorax and calcium injections were started, indicates that *such treatment does not influence the curve.*

Having answered this question, we proceeded to find out how the blood-sugar curve differs in tuberculous patients from that in healthy subjects. Figure 2, curve A is representative of a series of 20 similar curves in 62 tests. Their pulmonary disease is of the exudative-ulcerative type, as a rule of a rather short duration. The most characteristic feature of the curve is its descending limb. The highest point of the ascending limb is generally reached in 20 to 40 minutes. The descent which is, as a rule, finished within about two hours, is often 40 to 50 per cent lower than the starting fasting level.

In order to show that a possible hydration in the blood is not responsible for this type of blood-sugar curve, we have determined simultaneously in each blood specimen also its specific gravity. The curve C in figure 2 shows the corresponding curve obtained from these serum density determinations.

In figure 3, we show an average curve composed of ten different curves which are similar to curve A in figure 2. Such curves are the functional expression of the exudative-ulcerative type of pulmonary tuberculosis. Hence, it is obvious that we are dealing not with an occasional observation but with the principle particular to this type of tuberculosis.

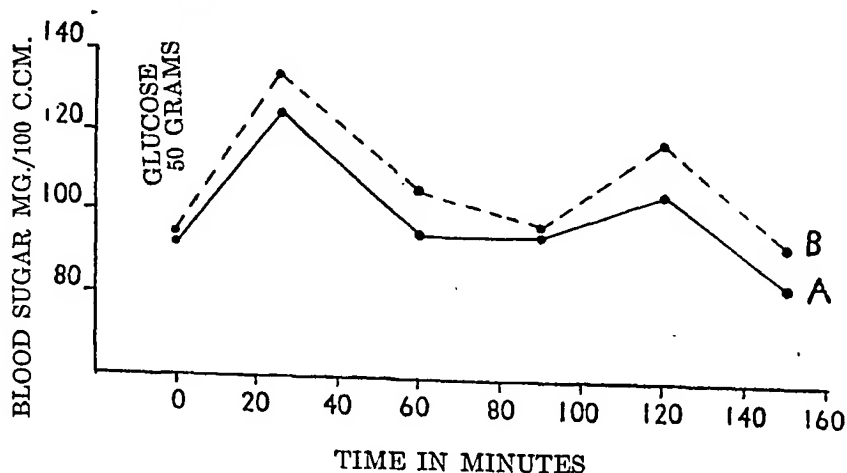


Fig. 1.—Influence of artificial pneumothorax and calcium gluconate injection treatment on the sugar-tolerance test.
Curve A.—Before treatment. Sedimentation rate (Cutler): 22 mm.
Curve B.—One month after above treatment. Sedimentation rate: 14 mm.

We tried to find what features were common to patients with this type of curve. We examined them also by means of percussion and auscultation, went carefully through their histories and studied their radiograms and blood sedimentation rates. Common to this type of tolerance

curve are the following features: A short history of the disease, sometimes but not invariably positive physical signs on percussion and auscultation, and a more or less fresh exudative-ulcerative process on the radiogram. We are under the strong impression that *there is a direct relationship between the rapidity and intensity with which the second limb descends and the acuteness of the pulmonary process.* The blood sedimentation rates (method of Cutler), however, frequently do not conform to this type of blood-sugar curve. The sedimentation rate is often normal but the blood-sugar curve is of a low descending nature. This is, however, not very surprising, as we find not infrequently an improvement of the sedimentation rate preceding the clinical and also the radiological improvement. It, therefore, appears that the blood-sugar curve may turn out to be a better indicator of the actual state of health than the sedimentation rate in this exudative type of phase of pulmonary tuberculosis.

In some tuberculosis cases we find quite another type of glucose-tolerance curve, as reproduced in figure 4.

As in figure 2, here also the specific gravity curve shows that this type of blood-sugar curve is not due to hydration. A striking feature of this curve, compared with figures 2A and 3, is that there is no descent of the second limb beneath the fasting level, and after two hours, is still considerably higher. The peak of 173 mg. per cent in the curve B is reached in 60 minutes. This type of curve resembles the mildest possible form of a diabetic glucose-tolerance curve. As these patients offer, however, no other clinical signs of true diabetes mellitus, no high fasting blood sugar, no sugar reaction in the urine, no acetone bodies, no polydipsia and

no polyphagia, we could classify this type of blood-sugar curves as 'potential diabetic' (lag curve). One other curve at our disposal shows such an impaired tolerance that one would classify it even as a severely diabetic one, but for the absence of all other clinical signs required

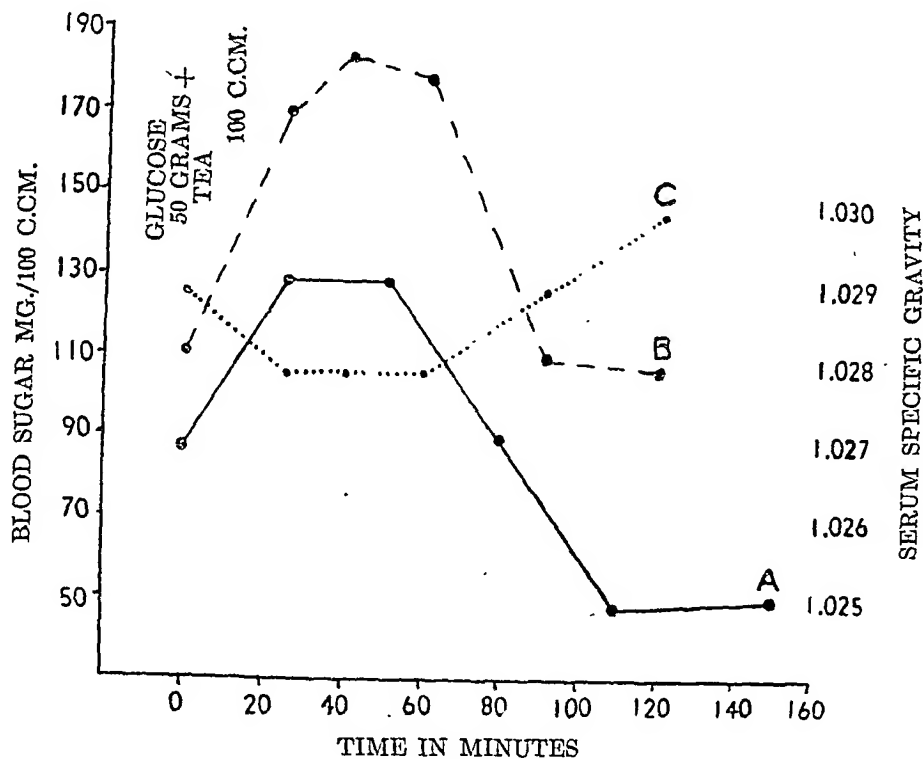


Fig. 2.—Effect of fibrotic healing of an acute exudative process on the blood sugar curve.

Curve A.—Taken one day after admission: very low descending limb, by nearly 50 mg. per cent lower than fasting level. Sedimentation rate: 22 mm.

Curve B.—Taken seven months later, after primary artificial pneumothorax 7 months ago and phrenic crush 2½ months ago. No descending limb present, but the fasting level and also the peak are higher than in curve A. Sedimentation rate: 8 mm.

Curve C.—Blood specific gravity curve taken simultaneously with curve B.

for the diagnosis of a genuine diabetes mellitus. It is a case of an apparently healed tuberculous lesion with extensive fibrosis. We show this curve in figure 5.

Among our 62 curves, we have seventeen of this potential diabetic type. We reproduce in figure 6 a curve which is constructed by combining these seventeen, and which shows the same characteristics as figures 4 and 5.

Again, we attempted to find what factors were common to these cases, by means of case history, physical and radiological examination and blood sedimentation rate. Common to them is the more or less long history of tuberculosis, with or without a history of diabetes in the family, a radiograph showing a proliferative fibrotic process with foci of calcification and, lastly, on clinical examination, a rather inactive process which has more or less settled down (see also figure 2, curve B in comparison to

curve A). The sedimentation rate in cases of this type is often low, but sometimes also high because of the secondary sepsis in the dilated bronchi.

There are in our sanatorium also many transitional cases, which were acute and exudative-ulcerative on admission, but want to heal in a proliferative manner after a number of years.

with fresh exudative processes, the corresponding blood-sugar curve characterized by its low descending limb. Figures 2 and 7 show instances of such transitional curves. They are, of course, of the greatest importance to our subject; forming the link, as they do, between the two extreme curves, they appear to afford strong support for the views expressed here.

If a fresh process is grafted upon a healed fibrotic one, it is natural that the sedimentation rate expresses mainly the active fresh component, and is high. The blood-sugar curve, however, is an expression of both the anatomical processes, the old and the new one, although it is admitted that knowledge of the simple, uncomplicated extreme curves is required to enable the reading and interpretation of these mixed curves.

There is still a fourth type of curve, which we call the 'saddle-form'. We have obtained 8 such curves from our total of 62 curves. They differ from the standard tolerance curves by the dip and sometimes also by a prolongation. Such 'saddle-curves' are mentioned in the literature as a result of a slow rate of digestion and absorption, for instance, after mixed meals such as sugars with much fat (Harrison, 1937). There are other observations on such curves by Tunbridge and Allibone (1940). Amongst 92 patients suffering from various diseases, these authors found the so-called 'hump-effect' taking place in 14 patients. Amongst 42 healthy persons, however, only one gave a slight degree of 'humping'. Similar effects have been observed by Noltie following the intravenous administration of dextrose in rabbits, and such effects were abolished after a small dose of insulin. Although the 'hump-effect' is not quite the same as our 'saddle-curve', we believe these fluctuations of the

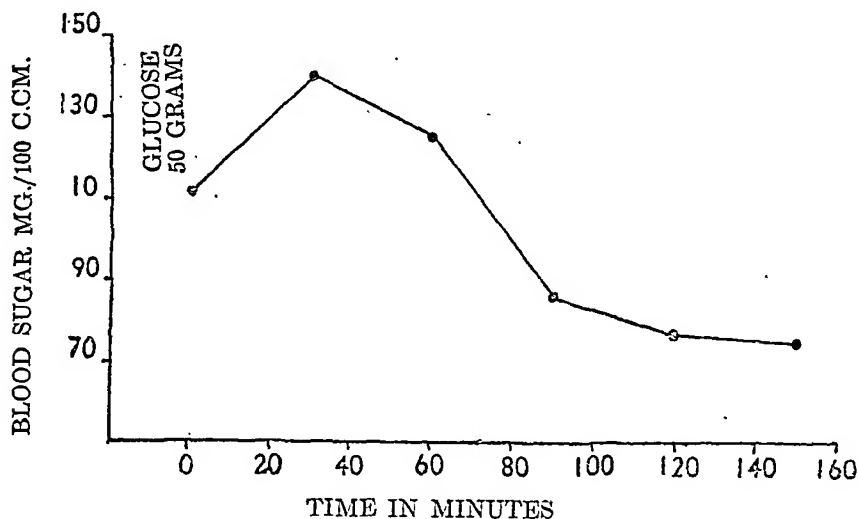


Fig. 3.—Curve composed of 10 different identical curves from patients suffering from acute exudative pulmonary tuberculosis. Same as in figure 2, curve A.

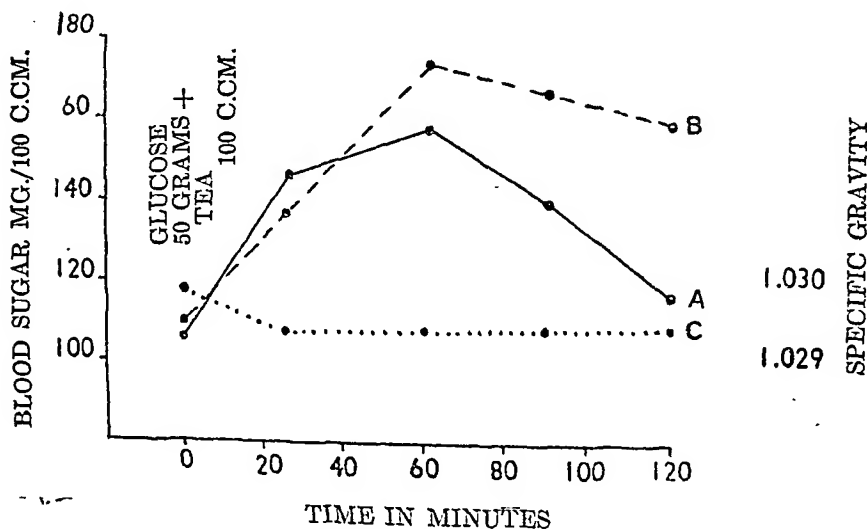


Fig. 4.—Progress of healing of an old-standing fibrotic process, after phrenic crush, gold and calcium injection.

Curve A.—Four days after admission with fresh infiltrations and exudate. Sedimentation rate: 24 mm.

Curve B.—After absorption of exudate and increase of fibrotic induration. Sedimentation rate: 11 mm.

Curve C.—Blood specific gravity curve, taken simultaneously with curve B.

The blood-sugar curve of such patients is also transitional according to their histopathological and clinical condition. *Vice versa*, cases which were on discharge more or less healed in an anatomical sense and presented accordingly a curve without a descending limb or without a prolongation, gave when re-admitted

blood-sugar level within one or two hours of oral and intravenous glucose, are not mere effects of delayed digestion or absorption. We also have an instance of a 'saddle-shaped' curve which has been straightened by insulin injections of 5 units thrice daily lasting for one month till one day prior to the blood-sugar test. We

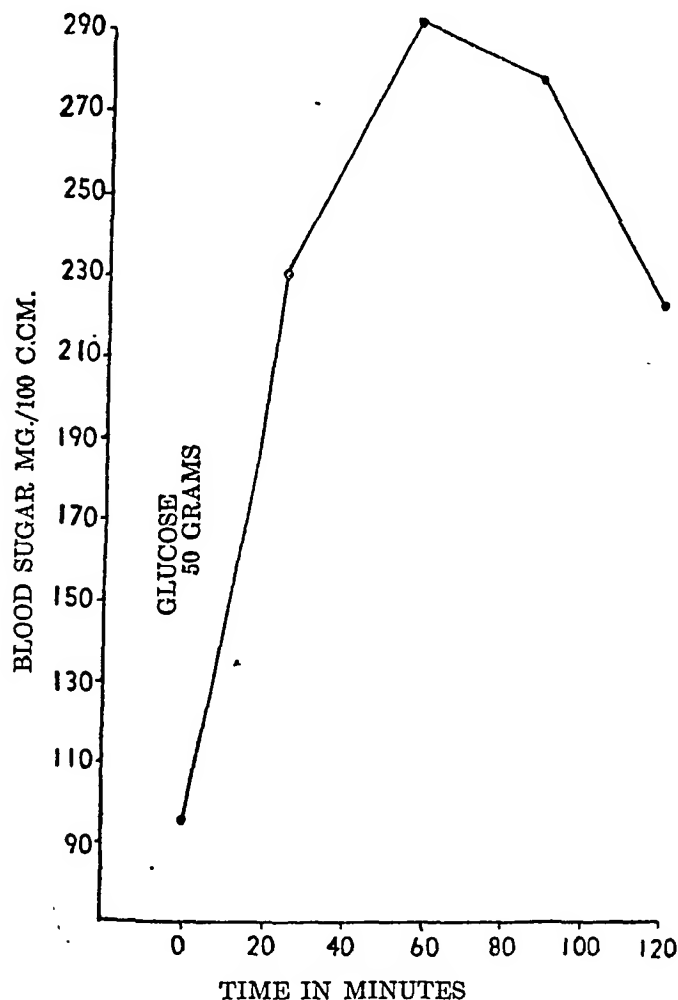


Fig. 5.—Blood-sugar tolerance curve resembling a diabetic one. No clinical signs of a genuine diabetes mellitus. No sugar in the urine before and $1\frac{1}{2}$ hours after intake of 50 gm. of glucose. *Radiologically*—fibrosis on right apex, right upper field and left hilar region. Sedimentation rate: 18 mm.

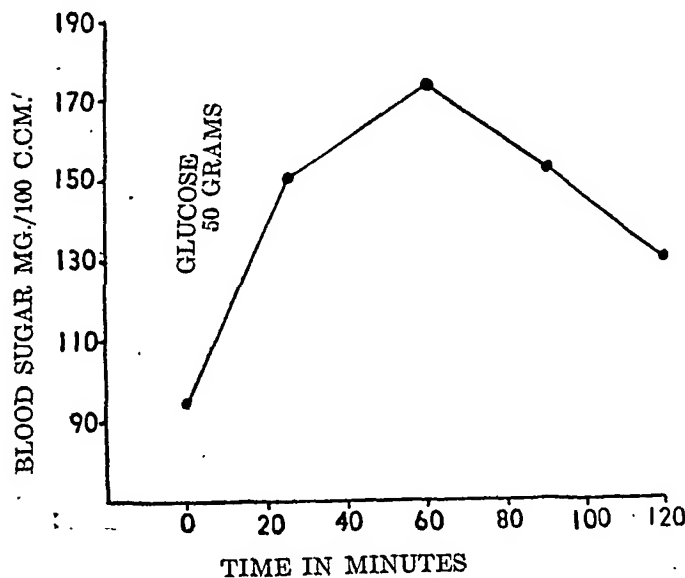


Fig. 6.—This curve is composed of 17 identical curves from patients suffering from more chronic, fibrotically healing forms of pulmonary tuberculosis.

consider our 'saddle-curves' like Tunbridge and Allibone's 'humping-effects', are possibly due to the balancing control of the endocrine glands, especially the adrenal glands, on the carbohydrate metabolism. To prove this, however, tolerance tests after oral and intravenous glucose on the same patient with saddle-shaped curve, should be carried out. We consider saddle-back curves as pathognomonic, although we are not yet in a position to relate them to a particular type of pulmonary tuberculosis.

Concluding, we would mention still another type of blood-sugar curve, the so-called 'flat curve', without, however, being able to offer any explanation as to its origin. We obtained such a curve in four female patients, two of whom showed signs of endocrine disorders. The description of one case is given in the legend to figure 8. The other showed signs of pluriglandular disturbance, mainly of the thyroid and the adrenals, resembling Addison's disease. She also gave a rather flat curve with a low fasting blood sugar, and had fibrotic tuberculosis lesions of 18 years' standing.

Nevertheless, the 'flat curve' is for the following reasons not likely to be an expression of the influence of the female sex hormones as such: six other female tuberculous patients among our ten gave no 'flat curve', but had curves characteristic of their type of tuberculosis. Furthermore, two other female patients with 'flat curves' presented no clinical signs of endocrine disorders whatsoever. On the other hand, we have met with a 'flat curve' in two male patients, who offered no signs of endocrine disorder. In the literature such 'flat curves' are mentioned in cases of idiopathic steatorrhœa by Thaysen (1935), and in his view they—like the 'saddle curves'—are also due to diminished absorption.

Discussion

In the almost total absence of physio-pathological studies of the tuberculous lung, it is not easy to explain our above findings. The only physio-pathological data elaborated with regard to the functions of the tuberculous lung are quite recent, and although well 'based on unimpeachable physiological and biological evidence' the conclusions are still of a hypothetical nature, as the author himself admits [Coryllos (Goldberg, 1939)].

In former investigations on the improvement of the blood-sugar tolerance of diabetics produced by means of oxygen-inhalation, Jacoby (1930) could show that it is in the *tissues* that an increased oxidation of carbohydrates takes place; and that it is also in the *tissues*, that an impairment of carbohydrate oxidation with

impaired sugar tolerance takes place, when carbon dioxide is inhaled instead of oxygen.

Coryllos *et al.* (1932) advance the conception that fibrosis goes hand in hand with tissue anoxæmia, produced by selective respiratory rest of the affected parts of the lung. Consequently, increased CO_2 and decreased O_2 in the arterial blood results. Similarly, within cavities without open bronchial outlet, manometric readings and gas analysis of air contained in them have shown a lowered oxygen and higher carbon dioxide content than in the outside air. Before, however, tissue anoxæmia is brought about in the fibrotic part of the lung, O_2 is absorbed by the cellular tissues; this absorption is more rapid than would be suspected and this because of the extraordinary amnity of the avascular *tuberculous tissues* for O_2 [Novy, Warburg (Goldberg, 1939)]. Absorption of O_2 produces a condition of anoxæmia in which tubercle bacilli cannot grow.

Our findings—former and present—are in keeping with these conceptions of Coryllos: The stage of absorption of O_2 by the affected fibrotic *lung tissue* would correspond with the increased sugar tolerance with the low descending limb of its curve. On the other hand, the stage of anoxæmia would correspond with the impaired sugar-tolerance curve (potential diabetic). The key to our findings would be in the *lung tissue itself*: when the tissue is absorbing O_2 and communicates it at the same time to the venous blood, the sugar tolerance is enhanced as in our former investigations after O_2 inhalation (Jacoby, 1930). When the tissue is anoxæmic and the venous blood contains more CO_2 , the sugar tolerance is impaired as in our former experiments on healthy people after CO_2 inhalation.

We are well aware that the greatest obstacle to this theory is the natural presumption that the compensatory action of the remaining healthy lung tissue should be able to make up for the impaired ventilation and circulation in the tuberculous tissue. We believe, however, that at this juncture it is too early to discuss this argument before having carried out accurate gasometric analysis on the subject, namely determinations of the CO_2 content or of the alkali reserve of the blood with van Slyke's apparatus and, further, determinations of CO_2 and O_2 in the expired air with Haldane's gas analysis apparatus on tuberculous patients of the different types. On the same patients, simultaneous blood sugar-tolerance tests in capillary and venous blood may also prove whether Coryllos' conception of the changed functions of tuberculous lungs and our explanations for the changed sugar tolerance of tuberculous patients are correct; namely, that the key

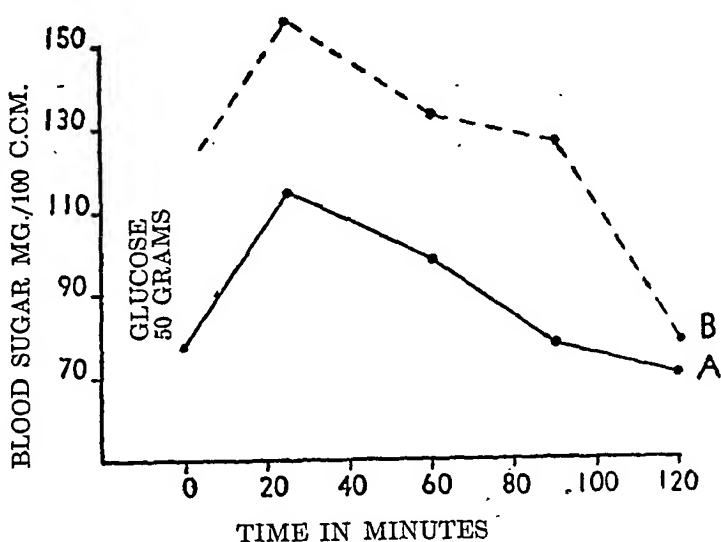


Fig. 7.—Effect of the clinically and morphologically flaring up of an already fibrotic process on the blood-sugar curve.

Curve A.—Improved condition after phrenic-crush, gold, calcium and tubercle filtrate injections. No descending limb. Sedimentation rate: 8 mm.

Curve B.—Patient re-admitted with hæmoptysis and fever. Now a descending limb is present. Sedimentation rate: 25 mm.

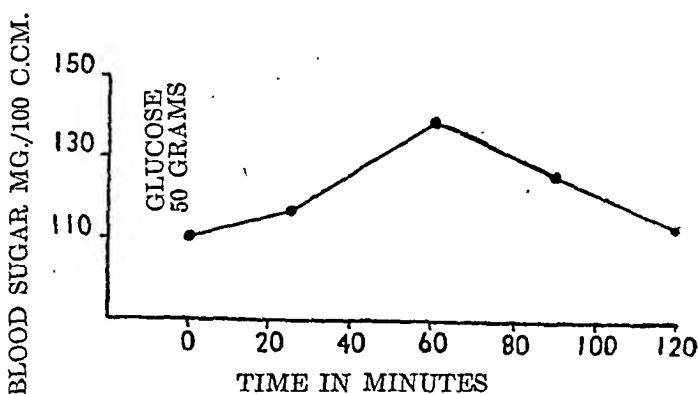


Fig. 8.—'Flat curve' of a 26 years' old female tuberculous patient with excessive growth of hair, abnormal to the patient's sex also, on the upper lip, chin, cheeks, lower legs. Her period is regular. Her pulmonary process is a mixture of extensive exudative-ulcerative-proliferative type. Sedimentation rate: 24 mm.

to these physio-pathological problems is mainly with the *tuberculous tissues*.

If we succeed by means of the above outlined experimental work in proving these relations, it would be obvious that they are the *direct* outcome of a tuberculous infection. There is, however, much clinical evidence, that 'tuberculosis is not solely microbic, *i.e.* depending only on infections and re-infections'.

Although in the present state of our physio-pathological knowledge of tuberculosis it is too early to draw conclusions, we may say that there is much clinical evidence to support the view

that 'phthisiogenesis is more a problem of pre-disposition than of bacterial infection' (Fishberg, 1932).

Summary

The not infrequent incidence of metabolic diseases in family histories of tuberculous patients, as well as the drop of tuberculosis incidence in diabetes since the discovery of insulin, and observations on the 'curative' effect of tuberculosis on diabetes, has led us to investigate the relationship between pulmonary tuberculosis and the carbohydrate metabolism by means of sugar-tolerance tests. We carried out 62 of them on 50 unselected afebrile tuberculous patients. We used the classical method of giving 50 gm. glucose orally. We distinguished with this method two different types of curves, one with enhanced sugar tolerance with a very low descending limb, the other with impaired sugar tolerance, sometimes resembling those of potentially diabetic patients. Morphologically, the former curve corresponds with cases of exudative-ulcerative pulmonary tuberculosis, the latter curve with those suffering from a more chronic fibrotic type. Morphological transitions between these two extreme types of pulmonary tuberculosis correspond functionally with their respective transitional sugar-tolerance tests. By means of determinations of the blood density, undertaken simultaneously with the blood sugar estimations on 45 patients, we could show that the form of the sugar-tolerance curve is definitely independent of and uninfluenced by the fluctuations of the blood density. An explanation of our findings has been attempted on the ground of recent physio-pathological findings on the tuberculous lung. A path for further studies for the elucidation of the functions of the tuberculous lung is indicated.

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SIMULTANEOUS BILATERAL 'EARLY INFILTRATION' IN A MIDDLE-AGED PATIENT

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In this country, most cases of lung tuberculosis when diagnosed are in a more or less advanced condition. Early detection, unfortunately, is a rare exception. It has been shown in western countries that the beginning of adult tuberculosis, the tertiary stage according to Ranke or the re-infection stage according to others, is very frequently located in the posterior-superior sub-apical region. Pathologically, it is a more or less extensive, exudative infiltration. This observation challenged the earlier conception of an insidious tubercular onset in one or both apices, which is unfortunately still deeply rooted in the minds of many practitioners. Periodical and serial x-ray examinations of certain professional groups, especially of hospital staff, offered the opportunity to detect the very onset of the disease in persons who were proved to be healthy in previous x-ray examinations and appeared even so at the time of detection. Burrell warns us 'that no signs may be found even by an expert in a case of extensive disease, and that he may be faced with a legal action for negligence if he has based his negative diagnosis on the absence of physical signs and has not had an x-ray taken'. The statement that the onset of the disease might take place in the sub-apical region had already been made by Ewart (Fishberg, 1932), Fowler (Fishberg, 1932), Gekler (Fishberg, 1932) and Wessler (Fishberg, 1932). To Assmann (1923), however, the credit must be given for investigating these sub-apical exudative patches in periodical and serial x-ray examinations, emphasizing that, but for the x-ray detection, many of these cases would have been overlooked, as clinical signs and symptoms were completely absent. His term 'early infiltration' (Assmann focus) for this phenomenon has been accepted by phthisiologists. Since then, innumerable communications have dealt with this subject. If I venture to add the following case, I may put forward 4 reasons, viz. (1) The relative rarity of detection of an 'early infiltration' in this country with close following up for three months, (2) the exceptional late appearance, (3) the hereditary late susceptibility and (4) the simultaneous appearance of lesions on both sides.

The patient, a male Hindu, 46 years old, is a member of the medical staff of a general hospital. He had

PLATE I

SIMULTANEOUS BILATERAL 'EARLY INFILTRATION' IN A MIDDLE-AGED PATIENT :
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Fig. 1.



Fig. 2.



Fig. 3.



Fig. 1.—Shows abscess cavity with fluid-level in the peripheral part of the lower lobe of the right lung.



Fig. 2.—Shows skiagram taken on the 5th post-operative day after right lower lobectomy. The seventh rib is resected and smaller segments of 8 and 9 ribs have been removed with the lobe. The drainage tube with side holes is seen at the base. The upper two lobes are seen to be well expanded to fill gap caused by removal of lower lobe.



Fig. 3.—Photograph of specimen of resected lobe of lung. Shows abscess cavity and sinus leading out to the chest wall a part of which has been resected. Just above the scale is seen the diaphragmatic surface of the lobe and above the cavity the interlobar surface. To the left is the hilar aspect showing cut pedicle and surrounding cuff of lung.

cervical adenitis at the age of 14 to 16 years; otherwise he enjoyed perfect health. The family history reveals the following interesting data: his father died at the age of 56 years after suffering from lung tuberculosis for about 6 to 7 years; his father's sister died at the age of about 50 years from lung tuberculosis; one brother died at the age of 38 years from lung tuberculosis. They all enjoyed perfect health but for the last period of their lives.

The health of the patient was checked as a matter of routine at periodical intervals. Fluoroscopies of the chest were done in December 1943, February 1944 and at the beginning of May 1944. None of the three screenings showed signs of parenchymatous lesions, although at the time of the last examination in May, the patient complained of pain at the back of the left side. Another screening on 5th June, 1944, suddenly revealed an infraclavicular infiltration on the left side with a cavity, and some small, hazy patches at the corresponding region of the right side, confirmed by a photo taken the next day (figure 1, plate I). There was no doubt that these infiltrations and the cavitation of the left side must have developed during the course of the previous month. The patient noticed only little symptoms of activity, some cough and expectoration (positive), slight occasional pain, rare subfebrile temperature, the general condition being quite good.

For personal reasons the patient paid little attention to medical advice and took only a little rest. The second photo (figure 2, plate I) taken on 8th July, 1944, showed slight resorption of the exudative patches of the left side, and replacement by apparently more linear shadows: the cavity was unchanged. The small indistinct patches seen on the right side of the first photo, however, had developed into an irregular, confluent infiltration with beginning cavitation in the centre. Again the patient preferred an expectant policy until 7 weeks later, on 25th August, 1944, a third photo (figure 3, plate I) revealed a cavity at the right side of about the same size as that of the left side, the latter being unchanged. Although a little higher, the picture of the right side appeared almost as if reflected by a mirror from the left side. Then at last the patient entered the hospital. (Other clinical data are omitted as irrelevant.)

The interesting points of this case are:—

(1) The sudden appearance and rapid cavitation of a typical 'early infiltration', a rare observation unless periodical and serial x-ray examinations are performed, particularly among professionally exposed persons.

(2) The appearance of an early infiltration at an advanced age of 46 years, whereas generally these forms are observed at the age of 15 to 25 years (Fishberg, 1932).

(3) A distinct familial taint evidenced by three other members of the patient's family who became victims of tuberculosis at a relatively advanced age. According to Burrell (1938) '... the disease undoubtedly tends to run a similar course in some families ... in other families the disease may develop at about the same age in each patient. Thus, some families tend to have an early and others a late susceptibility to tuberculosis. In one family 2 brothers and 5 sisters died from pulmonary tuberculosis, their age at death being 30, 44, 65, 76, 76, 78 and 81. It is generally agreed that tuberculosis is not hereditary, but that some factor affecting resistance or susceptibility may be inherited'. According to Fishberg, 'family resemblance' in phthisis has been found in about 75 per cent of cases. According to Edel (Fishberg, 1932) and others, in 34.29 per cent of the

families the disease began during the corresponding age.

(4) The simultaneous appearance of similar bilateral lesions. When the disease was detected, there was already a cavity on the left side, whereas the right side showed only slight infiltration. The difference in time, if there was any, between the onset on the two sides is negligible, notwithstanding the earlier appearance of the left cavity. The fully developed picture of the disease as seen in the third photo gives no clue as to the priority of cavitation (and even less of the very onset) on either side. The so-called daughter-infiltrations (Redeker), however, appear later, and are easily distinguishable from the original 'early infiltration', at least for quite a long time in the course of the disease. In the present case no such distinction is possible. In spite of the earlier cavitation on one side, the brevity of the developing period and the final picture of the fully developed disease point to simultaneous appearance on both sides.

Summary

A case of pulmonary tuberculosis is reported, showing a bilateral, simultaneous 'early infiltration' in a patient of 46 years with familial late susceptibility.

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AN ANTI-TUBERCULOSIS SCHEME FOR AN INDIAN CITY

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MANY are now busy with post-war planning for medical schemes, which include schemes for anti-tuberculosis work, and frequent requests are being made for plans and suggestions about how to proceed, and enquiries as to what is required. This paper is to suggest a scheme for a city of about one lakh population.

Estimate of the tuberculosis problem

Before we draw up a plan for an anti-tuberculosis scheme, we should have knowledge about the problem which has to be faced in the town. Some idea can be obtained from the mortality statistics, but this will represent the minimum only, as experience and investigations have shown that only a proportion of deaths from tuberculosis is reported as such. Probably for most Indian cities, it will be found that the tuberculosis death rate will vary from 200 to 500 per 100,000 population. The usual estimate

of the number of people suffering from active tuberculosis compared with deaths is between 5 and 10 sick to one death. In India, owing to the rapid course of the disease, the lower figure is probably more correct, namely, 5 sick to one death. This will mean that in a city of one lakh population, there will be from 200 to 500 deaths per annum and from 1,000 to 2,500 people suffering from active tuberculosis. Any scheme therefore which is drawn up will have to take these facts into consideration.

Essentials for the scheme

In the plan for the city, there will be required a diagnostic service, facilities for treatment and isolation of infectious cases, and in addition, an organization to deal with the preventive side of the work, including propaganda and education. It is however absolutely necessary that all these parts of the scheme should be co-ordinated so that they work as a whole and not independently. For this purpose, there will have to be a chief tuberculosis officer for the city, but for a city of only one lakh population, he may also be in charge of either a clinic or a tuberculosis hospital.

(a) *Diagnostic service.*—The tuberculosis clinic provides the best form of service for diagnosis. In an ordinary Indian city, a population of 50,000 will provide plenty of work for one clinic. Each clinic will have on its books from 500 to more than 1,000 persons with active tuberculosis for whose supervision it will have to be responsible, apart from those under observation such as contacts; in addition there will be all the usual other work of a preventive and educational character.

In large cities with a number of clinics, it will be desirable to have a large and fully equipped clinic, and others as subsidiary ones; five clinics could form a group of this nature. But in a town of about 100,000 which would need only two clinics, probably it would be better for both to be of equal standing. Some of the investigations, which in a large city would be done at the central clinic, can in a smaller town be done at the tuberculosis hospital.

A suggested plan for a clinic was given by Frimodt-Møller (1939), the actual plan drawn being intended for a hospital compound where x-ray facilities were already available, but suggestions were also made for the modification of the plan to include an x-ray department.

An alternative plan now suggested is shown in the figure. The rooms in this plan are the minimum, if the full work expected of a modern tuberculosis clinic is to be carried out. The wards for temporary observation are put upstairs to save the ground space which in a town may be expensive, but if sufficient space is available they may be put behind or to one side of the main building. It is difficult to give an estimate for the building which will hold for all parts of India, but it should generally be

possible to put it up and equip it for about Rs. 50,000, allowing for the increase of prices due to war conditions.

The staff of the clinic will be as follows: 1 tuberculosis officer, 1 assistant tuberculosis officer, 2 health visitors, 1 x-ray technician, 1 laboratory technician, 1 dispenser, 2 clerks, 2 peons, and 1 sweeper.

The cost of this staff and of contingencies, such as films, drugs, laboratory apparatus, stationery, will be about Rs. 20,000 to Rs. 25,000 a year. The running cost will therefore work out at about 8 annas per head of the population per year. This may seem a high figure, but the expenditure can be viewed from a different angle. It may be generally estimated that to treat a patient in a tuberculosis hospital or sanatorium will cost the community, either from private or public funds, about Rs. 900 a year. If the clinic can therefore save 30 people a year from developing tuberculosis requiring institutional treatment, it will save for the community the whole of its cost of running. This is certainly not an impossible figure, and a clinic properly run should be able to save far more than this number, and therefore will not only pay for itself but actually will be an economic benefit to the community as a whole.

(b) *Institutional treatment.*—The minimum hospital or sanatorium bed accommodation for tuberculosis cases is usually reckoned at one bed per tuberculosis death per annum. Therefore in a city of one lakh population, assuming a minimum death rate of 200 per 100,000, there should be at least 200 beds for tuberculous patients. If possible, this hospital should be outside the crowded areas of the town, but it should be easily accessible. The capital cost for such a hospital may be calculated as about Rs. 1,500 per bed, i.e. about Rs. 3,00,000, and the annual running expenditure will be about Rs. 1,80,000. It may not be possible for a town to begin with a hospital of 200 beds, but a smaller beginning may be made with 50 to 75 beds, provided the plans permit of extension, when this becomes possible.

(c) *Prevention, education and propaganda.*—The burden of tackling the tuberculosis problem in a city rests with its public health department. In this, it will use the clinic and the hospital, but the responsibility must not fall on these only. The organization of public opinion by various methods such as the radio, the press, lectures and school propaganda, will belong primarily to the public health department, as also the securing of funds for the institutions.

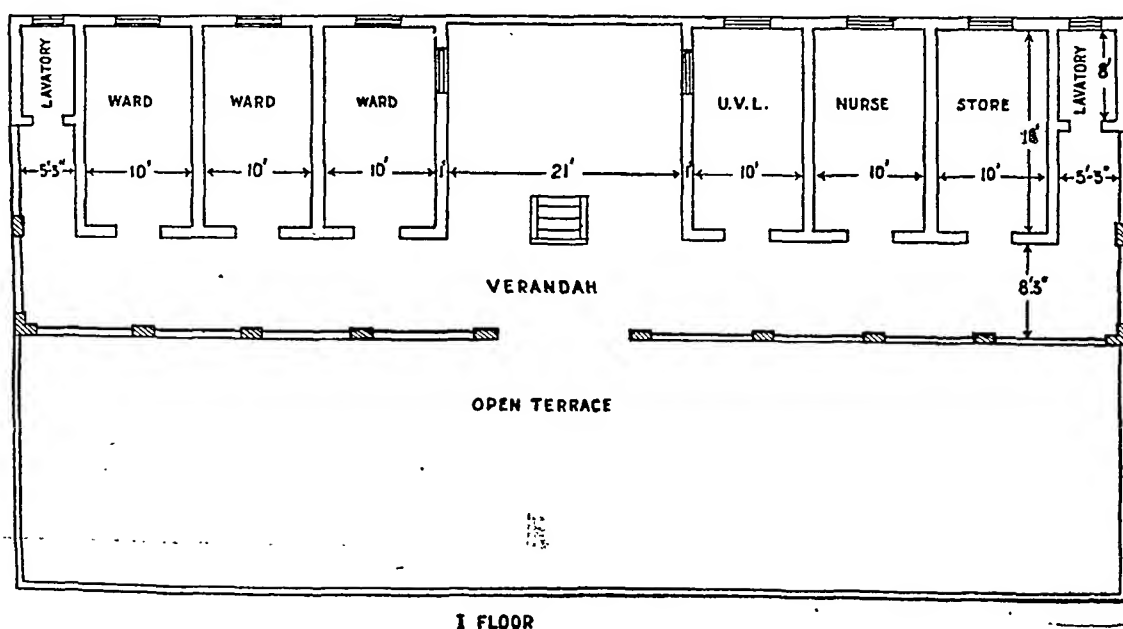
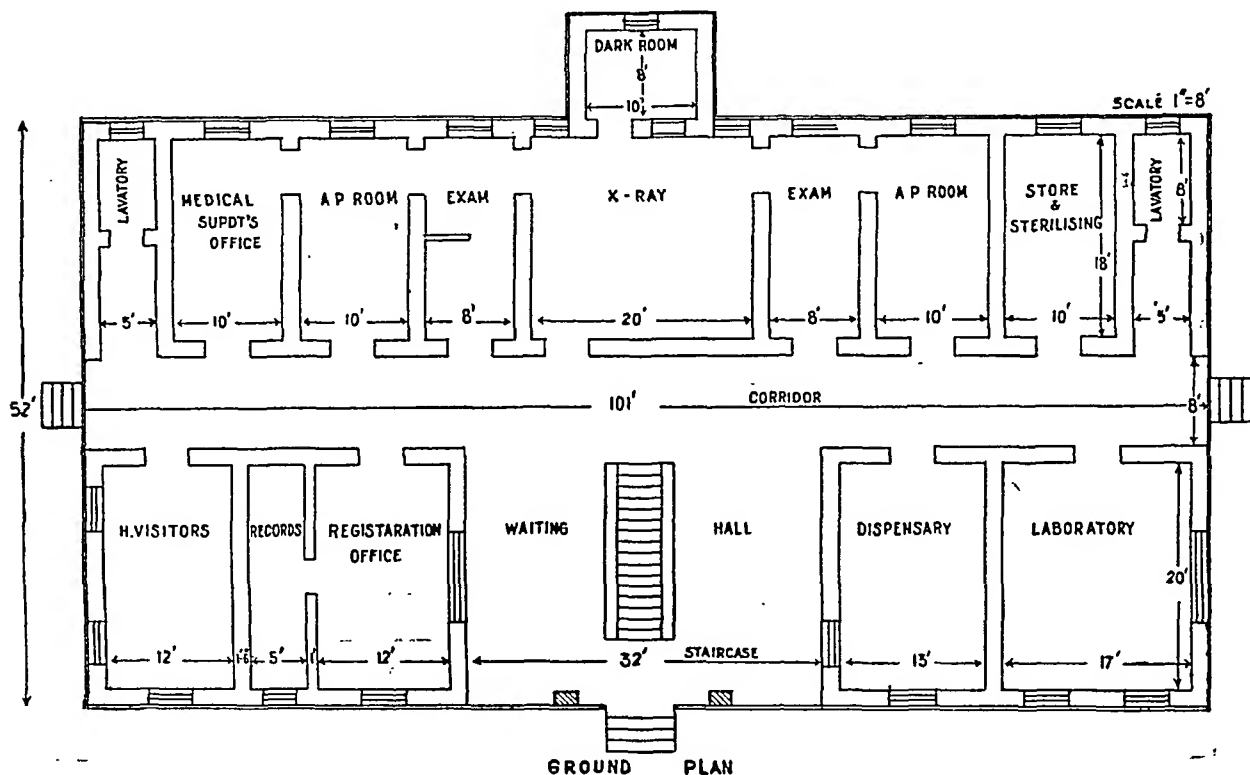
The clinic will not only be concerned with diagnosis, but will also play a large part in the preventive work. When there are only 200 beds in the hospital, it will mean that from 300 to over 1,000 patients will be under the care of each clinic, residing in their own homes. This will require a properly organized home treatment scheme, if further spread of infection is to be prevented. Another important part of

the clinic's preventive work is examination of contacts of 'open' cases.

It will not be possible nor desirable that the staff of the clinic should be alone in all this preventive organization, but there must also be

is necessary for their comfort and well-being, together with facilities for preventing spread of infection, such as a separate sleeping shed if no other separate sleeping place is available. The care of the families, particularly those

TUBERCULOSIS CLINIC



won the co-operation of private practitioners and of the general public. Tuberculosis committees formed from among the public and associated with the clinics, will be a necessary part of the anti-tuberculosis organization. On them will fall much of the responsibility for seeing that the sick, specially those at home, have what

where the bread-winner is sick, must be seen to by the committee, and in some cases, the finding of accommodation for children where the mother is sick. The after-care for ex-patients, such as providing suitable employment, extra food and milk and so on, will be another function of the tuberculosis committee.

The tackling of the tuberculosis problem in a city is no small task. The mere starting of a clinic or a tuberculosis hospital is only one small part of the scheme, and headway against the disease will be made if all parts of the anti-tuberculosis scheme are brought into play. There must, therefore, be a well-thought-out plan, well directed from the head, and well co-ordinated in all its several parts. Such a well-directed campaign should be able to reduce the tuberculosis death rate in a city from its present rate of 200 to 500 per 100,000 to a figure similar to that in western cities, namely, from 40 to 80 per 100,000 within about 15 or 20 years. Here is a challenge, an aim and a hope for every city health department in India.

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THE NORMAL MOVEMENTS OF THE COLON AFTER BARIUM MEAL IN INDIANS AND EUROPEANS

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DURING a radiological study of the intestinal tract in tuberculous patients, it was noticed that the barium passed more rapidly through the colon in Indian patients with no signs of intestinal tuberculosis than was expected from the findings reported as normal for Europeans (Frimodt-Møller, 1943). It was thought that the cause might be found in the different types of diet used for Indians and Europeans, but in the absence of a control material of healthy persons in India, no evidence in support of this hypothesis could be provided. The question has now been followed up by examination of a series of Europeans and Indians, apparently healthy, and the result is reported below.

Three aspects of the problem will be considered: first, is there any difference in the normal movements of the colon in between Indians and in Europeans living in India?

Secondly, do the Europeans in India differ from Europeans in the west? And lastly, is there a difference between apparently healthy Indians and Indian patients having intestinal tuberculosis?

1. Method and material

The persons to be examined were given 6 ounces of barium sulphate in the early morning. The position of the head of the barium column was recorded after 4, 6 and 10 hours, a final examination being done after 28-29 hours. No enema nor laxatives were given prior to the examination, and no restriction was imposed with regard to exercise or work; a light breakfast was allowed after the first examination and lunch after the second.

Members of the sanatorium staff, doctors, nurses, wardboys, *ayahs*, clerk, etc., and persons visiting the sanatorium, volunteered readily for the barium examinations. Care was taken to exclude anybody having a past history of gastric or intestinal disorders, or with a history of tuberculosis; further, fluoroscopy of the lungs in all cases revealed nothing abnormal. In all, 78 persons were examined, being distributed as follows:—

	Males	Females	Total	Mean age (with standard error)
Europeans ..	9	16	25	39.96 ± 2.18 years
Anglo-Indians ..	4	4	8	
Indians ..	35	14	49	29.49 ± 1.01 "

As no significant differences were found between the two sexes, males and females have been considered together. The four Anglo-Indian ladies who took European diet have been included in the group denoted in the following as 'Europeans'.

2. Indians compared with Europeans living in India

The distribution of the persons examined with regard to the position of the meal head of the barium column at the different periods of observation is given in table I.

TABLE I

Frequency distribution of apparently healthy persons according to position of the head of barium column

Position of head of barium column	Europeans (29 examined)			Indians (49 examined)		
	4 hours	6 hours	10 hours	4 hours	6 hours	10 hours
Ileum	3	8
Cæcum	5	2	1	..
Ascending colon	6	1	..	4	1	..
Hepatic flexure	3	3	..	3	2	..
Transverse colon	4	5	2	4	3	2
Splenic flexure	2	9	8	15	15	9
Descending colon	5	4	6	7	10	4
Iliac colon and beyond ..	1	7	13	6	17	34

Table I, which forms the basis for the following conclusions, shows only a little difference between the groups examined, the barium having advanced a little further in the Indians than in the Europeans. For the purpose of testing the statistical significance, the findings related to the descending colon have been recorded in table II. The differences found are so small that they are statistically insignificant and may therefore be only accidental.

TABLE II

Europeans and Indians compared with regard to filling of the descending colon

Observation period, hours	Europeans (29 examined)		Indians (49 examined)		Signi- ficance test*
	Cases with barium in descending colon		Cases with barium in descending colon		
	Num- ber	Per cent	Num- ber	Per cent	Per cent
4	6	20.7	13	26.5	0.756
6	11	37.9	27	55.1	0.219
10	19	65.5	38	77.6	0.376
Combined P ..					0.490

* Where nothing else is stated, the significance of the observations was estimated by means of the Chi-square test, using Yates' correction for continuity in case of four-fold tables.

Observations were considered to be significant when $P < 0.05$ (marked *), and highly significant when $P < 0.01$ (marked †).

When, however, the findings at the 28 hours' observation are considered, which show the position of the tail-end of the barium column, a marked and significant difference is found as the barium has moved considerably further down the colon in the Indians than in the Europeans; the proximal part of the colon being

As the cases showing the most advanced position of the barium at 28 hours were the same cases in which it had moved furthest at the earlier hours, it seems reasonable to conclude that the small difference noticed between the groups during the first 10 hours also represents a real difference and not merely a chance happening. Whether the difference observed is due to a racial factor or to the different types of diet or something else is difficult to say, though it seems natural to give the dietary factor a great deal of the credit.

Since the two groups were not composed of persons of the same average age, this fact could perhaps afford some explanation of the difference found. Each group was therefore analysed as to a possible association between age and speed of barium. While the Indians, when divided into two sub-groups of persons below and above 30 years respectively, showed no difference at all, the Europeans, as may be seen from table IV, showed more rapid movements of the colon in

TABLE IV

Age related to filling of the descending colon in Europeans below and above 40 years

Observation period, hours	Age < 40 years (15 examined)		Age > 40 years (14 examined)		Signi- ficance test
	Barium in descending colon		Barium in descending colon		P
	Num- ber	Per cent	Num- ber	Per cent	
4	5	33.3	1	7.1	0.099†
6	7	46.7	4	28.6	0.267†
10	11	73.3	8	57.1	0.299†
Combined P ..					0.138

‡ Estimated by Fisher's (1941) exact method.

TABLE III

Position of the tail-end of barium at 28-29 hours

	Europeans‡		Indians		Significance test
	Number	Per cent	Number	Per cent	
Cæcum ..	15	66.7	12	28.6	P 0.0104*
Ascending colon ..	3		2		
Transverse colon ..	5	18.5	12	24.5	
Descending colon and beyond ..	4	14.8	17	34.7	
Colon empty ..	0	..	6	12.2	
TOTAL ..	27	100.0	49	100.0	

‡ Two cases not examined.

filled in only 28.6 per cent of the former group against 66.7 per cent of the latter, and 12 per cent Indians having already passed all their barium (table III).

the group of younger persons than in the older one. The number examined in the two sub-groups are, however, so small that the differences do not reach the level of significance.

Comparing the Europeans below 40 years of age with the group of Indians of table II, it will be seen that they represent very much the same findings. On the other hand, the Europeans of 40 years of age or more have slower movements than the Indians, and in this instance the difference is significant (table V).

TABLE V

Comparison between Europeans above 40 years of age and the whole group of Indians with respect to filling of the descending colon

Observation period, hours	Europeans (14 examined)		Indians (49 examined)		Significance test† P
	Number	Per cent	Number	Per cent	
4	1	7.1	13	26.5	0.116†
6	4	28.6	27	55.1	0.073†
10	8	57.1	38	77.6	0.122†
Combined P ..					0.0304*

† Estimated by Fisher's exact method.

From this observation, it seems reasonable to suspect that the difference between the Europeans and Indians, though small, may be partly explained by the different age composition of the two groups; had the difference been caused solely by a dietary or racial factor, it should have been reflected in an equally clear difference between the Indians and the group of younger Europeans. It is quite possible that the difference associated with age, is a matter of difference of exercise, the older group of Europeans being of more sedentary habits than the younger Europeans and the Indian group.

Further analysis with respect to age of the findings of table III showed no relation between the position of the barium at 28 hours and different ages, either in Indians or in Europeans. Summarizing, it may therefore be argued that there appears to be a racial difference, particularly at the late (28 hours) observation period, and this can possibly be attributed to the different types of diet, while the less pronounced difference observed during the first 10 hours to a certain extent may be caused by a difference in the age composition of the two groups.

3. Europeans in India compared with Europeans in the west

Turning now to the question whether Europeans domiciled in India present any difference from Europeans in the west, it is clear from table VI, that there is a marked difference between the present series and one studied by Brown and Sampson (1930) in the course of their classical work on intestinal tuberculosis to which reference was made in my first report,

TABLE VI

Europeans examined by Brown and Sampson, U.S.A., compared with Europeans living in India (Arogyavaram)

Series	Number examined	Cases with barium in descending colon at 6 hours		Significance test P
		Number	Per cent	
Saranac Lake, U.S.A.	89	7	7.9	P < 0.001†
Arogyavaram, India.	29	11	37.9	

It is also evident that the Indian group, of which 55.1 per cent had barium in the descending colon at 6 hours, is quite at variance with the American findings.

In order to compare the present series with more general figures for the average rate of progress of barium in normal persons as stated by various authorities and summarized in table VIII, it has been estimated at what time the head of the barium column in the average European and Indian reached certain levels of the colon, such as the cæcum, the hepatic flexure, etc. This was done by estimating the times for 50 per cent of the cases by linear interpolation in table VII, which shows the percentage of cases in which the meal head had reached or passed these points at the three periods of observation. The times heading the columns of table VII indicate the mean interval in hours between ingestion of the barium and the individual examinations. The times for examining the 78 cases were normally distributed about their means within each of the three observation periods, the means having the following values:—

Observation period	Mean time interval (with standard error)
4 hours	4 hours 19 minutes \pm 1.65 minutes
6 "	6 " 23 " \pm 2.01 "
10 "	10 " 52 " \pm 2.29 "

For the present purpose, graphical interpolation as shown in the figure would be sufficiently accurate. The results are given in the last two columns of table VIII. The times given for the barium to reach the cæcum and the hepatic flexure must be taken with some reservation, as they fall in the interval before the first observation at 4 hours 19 minutes for which the shape of the curve is unknown and likely to differ considerably from a straight line; the other estimates, though not very accurate either, appear sufficiently correct to permit the conclusion that the present series of Europeans, as well as Indians,

show a faster passage of the barium than is generally regarded as the normal. Why a

difference can be found between Europeans living in the tropics and Europeans in more temperate climates it is not possible to say without further investigations; besides the difference in climate, there may be a multiplicity of factors such as change of environment, food, habits and exercise which play a rôle.

4. Motility of the colon in cases of intestinal tuberculosis as compared with normal controls

In the previous report on barium meal examinations of tuberculous patients, it was shown that patients with a filling-defect of the cæcum, typical of intestinal tuberculosis, had a significantly quicker passage of the barium than patients with an apparently normal colon. The difference was however so small that it was felt that hypermotility of the colon is such an uncertain symptom that it is not of much use in the radiological diagnosis of individual cases of intestinal tuberculosis. Relating these findings with the present observations on apparently healthy Indians, table IX shows that the latter do not differ appreciably from tuberculous patients with a normal colon, but they do show a significant difference from the patients having typical filling-defects; this difference is most pronounced at the 10 hours' examination. The difference previously observed between the two groups of patients (included also in table IX) was not only more marked than in the latter case, but it was found particularly at the 4 and 6 hours' examinations.

It can therefore again be concluded that hypermotility in cases of intestinal tuberculosis is not a very important nor specific symptom, and should be treated with caution as an aid for the x-ray diagnosis of intestinal tuberculosis.

It may not be out of place to add that in none of the 78 normal cases were observed any irregularities of the cæcal shadow comparable to the filling-defects characteristic of intestinal tuberculosis.

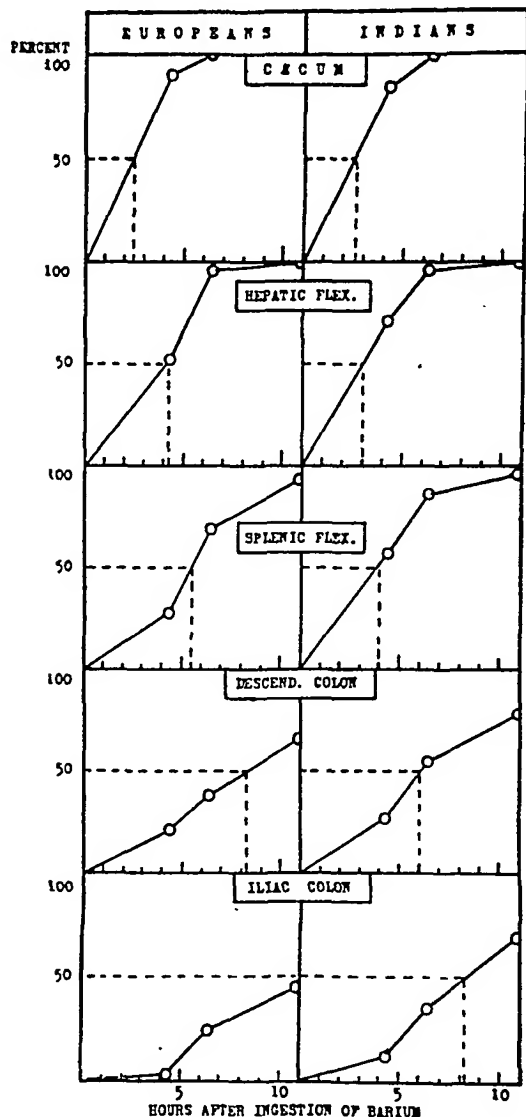


Figure showing percentage of cases in whom the meal head of the barium column had reached, or passed certain levels of the colon, plotted against time after taking the barium (vide table VII).

TABLE VII

Progress of barium column in Europeans and Indians as shown by percentage of cases in whom the barium had reached or passed certain levels of the colon

	Europeans						Indians					
	4 hours 19 minutes		6 hours 23 minutes		10 hours 52 minutes		4 hours 19 minutes		6 hours 23 minutes		10 hours 52 minutes	
	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent	Num- ber	Per cent
Ileum ..	29	100	29	100	29	100	49	100	49	100	49	100
Cæcum ..	26	90	29	100	29	100	41	84	49	100	49	100
Hepatic flexure ..	15	52	28	96	29	100	35	71	47	96	49	100
Splenic flexure ..	8	28	20	69	27	93	28	57	42	86	47	96
Descending colon ..	6	21	11	38	19	66	13	27	27	55	38	78
Iliac colon ..	1	3	7	24	13	45	6	12	17	35	34	69

TABLE VIII

The average progress of the barium meal (in hours) through the colon according to various authors

	Brown and Sampson, 1930	Starling (after Hurst), 1933	Wright, 1936	Best and Taylor, 1937	Shanks, Kerley and Twining, 1938	Present series	
						Europeans	Indians
Cæcum ..	4½ (3½-5)	4-4½	4½	2½	3	2½?	2½?
Hepatic flexure ..	6-6½ (5-8)	6½	6	4	5-6	4½	3?
Splenic flexure ..	9 (7-14)	9	9	6	12	5½	4
Descending colon ..	11 (8-16)*	11	11	8½	6
Iliac colon	12	12	< 10½	8½
Pelvic colon ..	12	18	18

* Lower end of descending colon.

TABLE IX

Comparison between (a) apparently healthy Indians, (b) Indian patients (pulmonary tuberculosis) with radiologically normal colon, and (c) Indian patients with intestinal tuberculosis (diagnosed radiologically)

(i) NUMBER OF CASES WITH BARIUM IN DESCENDING COLON

Observation period, hours	Number examined	Cases with barium in descending colon	
		Number	Per cent
		<i>(a) Healthy Indians</i>	
4	49	13	26.6
6	49	27	55.1
10	49	38	<u>77.6</u>
		<i>(b) Tuberculous patients with normal colon</i>	
4	93	19	20.4
6	83	34	<u>41.0</u>
10	93	79	84.9
		<i>(c) Tuberculous patients with intestinal tuberculosis</i>	
4	60	25	41.7
6	53	35	<u>66.0</u>
10	58	55	<u>94.8</u>

(ii) RESULT OF SIGNIFICANCE TESTS (P):

	(a) - (b)	(a) - (c)	(b) - (c)
4	0.543	0.149	0.008†
6	0.165	0.358	0.012*
10	0.391	0.011*	0.606
Combined P:		0.037*	0.004†

5. Conclusion and summary

By barium meal examination of 78 apparently healthy persons, 25 Europeans, 4 Anglo-Indians and 49 Indians, it was found that there is not much difference in the rate of progress of the barium shadow through the colon except after 24 hours when the Indians showed a definitely

faster movement than the Europeans. The reason may be sought in a difference in the types of diet taken by the groups though the small difference observed within the first ten hours may be partially due to a different age composition of the groups examined.

Both the Indians and the Europeans showed a marked increase of the speed of the barium as compared with figures given as normal for Europeans in the west. The average time for the barium to reach the hepatic flexure in Indians was about 3 hours, the splenic flexure 4 hours, the descending colon 6 hours and the iliac colon 8½ hours, the relevant figures for the Europeans being 4½, 5½, 8½ and in the case of the iliac colon more than 10½ hours.

The passage of the barium in Indian patients with pulmonary tuberculosis but with no affection of the colon compared well with that of the control group of healthy Indians, whereas patients with radiological evidence of intestinal tuberculosis (characteristic filling-defect of the cæcum) showed hypermotility of the colon, though not very marked.

Hypermotility is not a very important radiological sign in intestinal tuberculosis, and a diagnosis of this disease mainly based upon this symptom without the demonstration of filling-defect, should be treated with great reservation.

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LOBECTOMY FOR ABSCESS OF THE LUNG

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PULMONARY abscess is a serious disease which until recently has had a reported mortality of 30 to 60 per cent (Sweet, 1940 and Brunn, 1934). Ideas about its treatment have been in a rather confused state. Physicians and most surgeons tended towards an attitude of studied conservatism until developments forced their hands, or an arbitrary period of 2 to 3 months had passed when the disease was considered chronic and fit for surgical intervention. Even among these cases, the arbitrary limit between acute and chronic abscess was variously placed anywhere between 6 weeks and 4 months. Some surgeons relied entirely on postural drainage and bronchoscopic suction, while others were more in favour of earlier external drainage. In the last few years, some measure of standardization has appeared in the treatment of this disease, and it has been increasingly recognized that the earlier and more direct methods of surgical attack are achieving better results than the old conservative measures.

A recent experience, in which a chronic abscess of the lung which had previously been drained without success was cured by lobectomy in a fraction of the time usually taken after drainage, made us wonder if many of these cases may not be more successfully and expeditiously treated by primary lobectomy. On reviewing the recent literature on the subject, we find that from a welter of confusing thought some broad principles may be picked out, and certain rules of guidance established for the selection of the appropriate conservative or more radical measures in the treatment of pulmonary abscess. I shall first describe the case that stimulated this paper.

M. X. B., male, 22 years old, was brought to us in November 1943 by one of our patients. He gave a history that about 18 months before he had a sudden attack of pain in the right chest with high fever and cough. He was admitted to a hospital in Goa where after a few days a needle was inserted into his chest. He does not know what was found, but soon after he began to cough up blood and pus, and the temperature dropped to normal. Ever since, he has been coughing up foul-smelling pus and has been losing weight and vitality. In January 1943, he went to a large hospital in British India where a right phrenic avulsion was done without benefit. Thereafter he attended various hospitals without relief. When he came to us in November 1943 he used to have a low evening fever, cough with foul sputum and a general feeling of malaise. On examination, we found a pale flabby young adult with a dusky complexion. All his fingers were clubbed; there was a scar of phrenicotomy in the right neck; the heart and other systems were normal. There was impaired resonance over the base of the right lung laterally and posteriorly, with cavernous breathing. A skiagram showed a typical lung abscess in the periphery of the right lower lobe. Blood picture:—RBC 3.6 millions, WBC 7.4 thousands, Hb 68 per cent, polymorphs. 76 per cent, lymphocytes 18 per cent, eosinophils 4 per cent, monocytes 2 per cent. Kahn test negative; sputum negative for TB; urine normal.

A diagnosis of chronic lung abscess was made. He was admitted for surgical treatment. He was placed on postural drainage for a few days. The abscess was located in the periphery of the right lower lobe behind by careful fluoroscopy (figure 1, plate II). On 12th November, 1943, a 3-inch piece of the overlying 9th rib was resected. The pleura was found adherent, and the abscess was located by needling. The cavity was opened with the cautery and a fairly large opening made. A small amount of foul pus drained away. The finger could palpate a cavity about 2½ inches in diameter with rather firm walls. A penrose drain was inserted, the cavity packed with gauze, and the wound left open for drainage. Except for a fever of 102°F. the next day with bronchitic sounds in the healthy lung, all of which promptly responded to sulphapyridine, the post-operative course was uneventful. His sputum and cough rapidly subsided and external drainage diminished with a remarkable improvement in his general condition. He was sent home with a fistula kept open by a drainage tube two months after drainage, and asked to report after a month. He returned in February 1944 with foul discharge from the sinus and a return of cough and fever. A skiagram revealed the same unhealed cavity. It was decided that something more drastic had to be done. As the thick fibrous walls of the cavity could not be expected to collapse by another drainage operation, and as the cavity was peripherally situated, it was considered that a lobectomy offered the best chance of cure.

On 20th March, 1944, the lobectomy was carried out. General anaesthesia with intra-tracheal cyclopropane and oxygen was administered using controlled respiration. The sinus was first packed with gauze, a circular incision was made around the sinus, and the margins of the latter infolded and stitched over the gauze to prevent leakage. An incision along the 7th rib was then made on the postero-lateral aspect of the chest, and that rib resected. The pleural cavity was entered at the anterior end of the wound, and it was found that the middle lobe was free from the chest wall but there were dense adhesions between the lower lobe and the parietes, diaphragm and posterior segment of the middle lobe. The separation of the adhesions was a long and tedious process, the middle lobe being freed by cutting between clamps. A portion of the chest wall including part of the 8th rib was isolated with the lower lobe. The pedicle of the latter was then defined, and a lung tourniquet applied and tightened. A second tourniquet having been applied distal to the first, the lobe was amputated in between. The stump was oversewn with catgut and the cut ends of the bronchus and vessels covered over by a cuff of overhanging lung tissue. A drainage tube was placed with its tip below the stump and the chest wall repaired and closed. The patient stood the operation well except towards the end when the blood pressure dropped to a very dangerous level, and the operation was hurriedly concluded (see figure 3, plate II). He received 500 c.cm. of blood and 1,000 c.cm. of glucose saline during the operation and 500 c.cm. of blood after return to the wards. With the latter his general condition gradually improved. The drainage tube was attached to a Wangenstein suction arrangement to induce a negative pressure in the thorax and assist in the expansion of the remaining lobes to fill up the chest. The day after the operation he showed a temperature of 102°F. and dyspnoea which promptly responded to bronchoscopic suction, and with Cibazol the fever subsided in two days. On the 5th day, he developed a bronchial fistula as evidenced by air being continually sucked out by the suction arrangement and also some fluid in the lower chest. The upper two lobes had by now expanded considerably (figure 2, plate II). The discharge lessened rapidly and the tube was gradually shortened until a small sinus track was left communicating with the bronchus at the hilum. This finally closed in the 6th week after the operation, and the patient was discharged well.

The successful outcome of lobectomy in this case set us thinking whether a primary lobectomy might not have been a better thing to do for this patient. As the lobectomy wound had healed in 6 weeks it would have saved him a lot of time and the need of a second operation if resection had been undertaken in the first instance. In answering this question we must first consider what percentage of patients are cured by a simple drainage, what is the average time taken for cure, and how does the mortality of lobectomy compare with the simpler procedure to make it an operation worthwhile.

In a report of a series of 124 cases, Sweet (1940) has found that simple drainage cures 30 per cent, 26 per cent die in spite of the treatment, and about 43 per cent require subsequent operations to effect a cure. Of course, many of the above deaths are not due to the operation but are determined by the severity of the disease itself, the mortality attributable to the operation itself being about 7 per cent. Therefore, one sees that a simple drainage operation leaves 43 per cent of patients for a further operation to cure.

As regards the time taken by an abscess that has been drained to heal, the general experience has been about 2 to 6 months (Turner, 1934). Brunn (Betts, 1941) has reported an average period of hospitalization of 154 days for his series of cases treated by combined medical and drainage measures. The average time taken by a lobectomy wound to heal is six weeks (Turner, 1934).

When the mortality of lobectomy is considered, a report by Lindskoge (1944) of New Haven, is of interest. He records 14 primary pulmonary resections for lung abscess, with only one death (7 per cent mortality) and comments on the enormous saving of time and distress to the patient. All the 13 patients are cured and well. So it apparently appears that a primary resection of the lung should be preferred to drainage. Nevertheless, one has only to go more deeply into the question to realize that, as happens with all controversial methods of treatment, the truth really is that each procedure has its own indications, and that only when thus used are the ultimate results better than when one method is practised to the exclusion of the others. We shall therefore make an attempt here to indicate what plan of attack would yield the best results in pulmonary abscess.

All treatment should be based on a knowledge of pathology, and one may consider the pathogenesis and morbid anatomy of abscess of the lung before discussing its treatment. There are two main varieties of abscess which differ from each other in causation, pathology, and response to treatment—the putrid and non-putrid abscess, so called from the presence or absence of factor. The non-putrid abscess usually results from a pneumonia or pneumo-

nititis or septic embolism of the lung. The organisms concerned are pneumococci, streptococci, staphylococci, or other aerobic bacteria. There is an area of intense pneumonitis, and pus formation which is usually not well circumscribed. Cure occurs frequently without surgical intervention, or the patient dies from rapid progression. These abscesses do not often come for surgical treatment.

The putrid abscess usually begins as a gangrenous broncho-pneumonia, and is usually caused by aspiration of material from the throat, often after operations on the upper respiratory tract. The process begins with blockage of the lumen of a terminal bronchus and atelectasis of the lobule concerned. The latter becomes a nidus for organisms to grow upon, and the inflammation soon spreads to the peribronchial tissues, and leads to thrombosis of the bronchial and pulmonary vessels supplying the lobule, which run close to the bronchus. Necrosis of the lobule follows this deprivation of blood supply, and the process is most marked at the periphery of the lobule which is furthest from the vascular source. Thus, a putrid abscess always tends to occur at the peripheral parts of the lobe. The devascularized segment offers a favourable medium for the growth of anaerobic organisms which are responsible for the fætid odour of these cases. These abscesses do not tend to spontaneous regression, and often require surgery.

Once an abscess has formed, it may undergo resolution, progression to spreading pneumonitis and death, or burst into a bronchus or into the pleural cavity. The putrid abscess is less likely to burst into the pleural space, as the lesion early affects the outlying portions of the lobule, and so early leads to the formation of pleural adhesions. Empyema if present is more likely to result from a non-putrid abscess. When the pus finds a vent through the bronchus, if the drainage is adequate, the abscess heals like any other abscess in the body, assisted at times by postural drainage and bronchoscopic suction. If the drainage is not proper, the abscess becomes chronic, with surrounding fibrosis, atelectasis or bronchiectasis, and, when these processes have gone on for some time, even provision of good drainage does not succeed in curing the patient. Therefore, it will be realized that the institution of early and effective drainage is of the first importance.

If the pathology of pulmonary abscess as described above is kept in mind, it is not difficult to arrive at a rational plan of treatment. The first thing to realize is that the period of time that the abscess has existed is not an important factor in determining the treatment, as has been the practice until recently. More important are considerations such as the presence of spreading pneumonitis, adequate drainage from the bronchus, fibrosis, atelectasis, bronchiectasis or empyema. Therefore, it is not rational to divide cases into acute and chronic

by an arbitrary limit placed at so many weeks or months and apply conservative measures to the acute and surgical methods to the more chronic. If an abscess does not drain adequately from the bronchus, no matter whether it is only 2 or 3 weeks old, external drainage is indicated, if it is to be speedily cured and a long drawn out illness prevented.

Rather than divide abscesses into acute and chronic it is more useful to divide them into uncomplicated and complicated, and to plan the treatment accordingly.

Uncomplicated abscess

(a) Non-putrid abscesses have a tendency to resolution or cure with medical management, and should be treated with the sulpha-drugs, shortwave therapy, etc., in the first instance with the addition of postural drainage and bronchoscopic suction if discharge is coughed up. When no improvement is noted, surgical drainage is required.

(b) Putrid abscesses again should be treated medically to begin with, and the usual postural and suction methods used if draining through the bronchus. However, if it is not soon evident that sufficient drainage is established, there is already an indication for early external surgical drainage. Even at this early period, pleural adhesions are found, as can be understood from the pathology of this type of abscess. Careful localization of the abscess with the help of the radiologist will indicate where the adhesions are to be expected, so that the incision may be suitably placed. When the underlying pleura is found adherent, the abscess is located with a needle and opened with a cautery. As much of the roof of the cavity as can be safely removed without risk of entering the pleural space is removed, and the cavity packed with gauze, leaving the wound wide open. If no adhesions are found, obliteration of the pleural space is induced by packing the exposed space with gauze. After 3 to 5 days the lung has become sufficiently adherent to allow drainage of the abscess with safety. Sometimes the condition of the patient does not permit delay in opening the abscess, and in these circumstances it is not necessary to wait for obliteration of the pleural space. This may be obtained by stitching the visceral pleura to the chest wall over the segment to be drained before proceeding to open the abscess.

Uncomplicated abscesses are all cured by simple conservative measures or external drainage whatever be their duration.

Complicated abscess

These cannot be cured if treated on conservative lines.

(a) Associated with empyema: It is usually enough to drain the empyema according to the usual principles. Many of these patients are desperately ill and die, but some recover without further drainage.

(b) In the presence of marked fibrosis or bronchiectasis, a simple drainage operation cannot be expected to cure many cases. The cavities refuse to collapse because of rigid walls. These cases, we feel, are best treated by primary pulmonary resection, with much saving of time and more certainty of cure.

(c) Multiple abscesses in one or two lobes are difficult to drain satisfactorily and, if the patient's condition permits, a resection would be the best treatment.

(d) In the presence of surrounding atelectasis which does not clear up with bronchoscopic suction and medical measures, a lobectomy would certainly be indicated.

(e) If there has been one or more severe bleedings from the abscess, it would be wise to consider resection of the lobe rather than risk a fatal hæmorrhage after simple drainage.

We believe that by separating simple abscesses from abscesses with the complications enumerated above, we have a rational basis for planning out the most suitable treatment in any particular case. It is seen that by adopting pulmonary lobectomy or resection as the primary treatment in certain of the complicated abscesses, the patient is given a more definite assurance of cure and an enormous saving of time with only a slightly enhanced, if any, risk from the operation. Surgery limited to external drainage in all cases we have seen to cure only one-third of the patients, leaving over 40 per cent of the sufferers to undergo further operations, re-drainage, plastic, closure of cavities, thoracoplasty, and secondary lobectomy. Our patient, whose history has been recorded above, was certainly a candidate for primary lobectomy. With a history of 18 months, the presence of marked fibrosis around the cavity should have been expected, and the hope that external drainage would cure him should not have been entertained. However, a primary drainage in these cases may be justified only on the grounds that it reduces the virulence of the infection in the cavity and the seriousness of the post-lobectomy localized empyema that almost invariably follows resection for infected lesions of the lung.

Before ending I feel that I must acknowledge my debt to our anæsthetist, Dr. B. N. Sircar, without whose expert handling of the problem of anæsthesia I would not have been able to bring this lobectomy to a successful conclusion.

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[Note.—In response to an enquiry the author of this article states: 'This hospital is for the treatment of neoplastic diseases and we do not treat abscess of the

lung unless it occurs in one of our patients. My experience of the operative treatment of this condition is limited to the one case here reported.' The article is based mainly on the study of the literature on the subject.—*EDITOR, I. M. G.]*

TROPICAL EOSINOPHILIA

By I. G. K. MENON, M.B., B.S.

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FRIMODT-MÖLLER and Barton (1940) described a clinical condition characterized by leucocytosis and eosinophilia and associated with cough, fever, loss of weight and strength, blood-stained sputum or frank hæmoptysis and asthma or bronchitis in varying combinations and degrees. These cases gave an x-ray picture of the chest closely resembling that of miliary tuberculosis. The common pattern of signs and symptoms, the distinctive blood picture, the absence of any laboratory finding suggestive of tuberculosis and the uniformly good prognosis combined to justify the labelling of these cases as a new syndrome.

An allergic origin was suggested chiefly on account of the eosinophilia. As their title 'A pseudo-tuberculous condition associated with eosinophilia' suggested, the problem was viewed from the standpoint of the specialist in tuberculosis, and it was definitely concluded that it had no connection with tuberculosis.

In 1943, Weingarten described a similar condition under the name Tropical Eosinophilia. In addition to the earlier findings, he pointed out the splenic enlargement occurring in the febrile period, the acceleration of the sedimentation rate of blood, and the striking therapeutic results obtained in these cases by treatment with the aromatic arsenicals by intravenous, intramuscular or oral routes. He was against the theory of its allergic origin and concluded that 'the influence of the environment (meaning residence near the sea) as an ætiological factor is therefore unquestionable'.

Cases have since then been reported by Treu (1943), Simeons (1943), Chaudhuri (1943), Chakravarty and Roy (1943), Shah (1943) and others. All these cases are reported from India. Emerson's case (1944) was a non-Indian but he had stayed in India for 4½ years.

Bass reported in 1941 from America a similar condition in three children, with general adenopathy, leucocytosis and extreme eosinophilia. Of the three, one died of intercurrent illness, one ended in complete recovery after several years and one child under observation at the time of report had got over the febrile period and was in good health with a normal W.B.C. count but still persistent eosinophilia. He gave data of four cases from Havana showing a similar clinical picture. These cases closely resembled the Indian condition, excepting for the new feature of general adenopathy. Parsons-Smith in 1944 described it in an English airman who had never been in India but had been in Egypt for 10 months. Six injections of neoarsphenamine cured him.

An analysis of the findings in 8 cases seen during the course of the year in the Institute is given in tables I and II. They agree with the earlier observations on many points.

Age incidence.—It is more common in the decades below 30 and specially in the group 20 to 30. Males are more often affected than females.

Symptomatology.—A low, often irregular, fever persisting over several weeks was the most constant finding in this series. Generally this occurred at the commencement of the illness. Cough was present in most of the cases but it was of a dry irritant type, and in only one out of 8 was enough sputum available for examination. The lung signs were variable and present only for a brief period, sometimes only for a day or two. The x-ray picture was more persistent and typical. In addition to the scattered small foci throughout the field, some of the cases showed unusually marked hilar shadows. Splenic enlargement was present in 2 out of the 8 cases (nos. 1 and 2). Two patients (nos. 5 and 6) did not show any splenic enlargement during the whole febrile period when they were observed. Enlargement of the liver was noticed in 2 cases; in case 2 it persisted throughout a period of 16 months, and came down in size with arsenical injections at a much slower rate than the spleen. In case 7, the liver was palpable 1 inch below the costal margin during the first week of fever. Emaciation and loss of weight were present in all but one (case 8). In case 2, diarrhoea was present at the onset of illness, case 4 had enlarged groin glands while case 8 was remarkable for his feeling of fitness and the complete absence of any symptoms in spite of the frequent occurrence of albumin and granular casts in his urine, with the occasional finding of high blood pressure. Whether these findings in individual cases have any connection with the syndrome proper, or they just co-existed in these patients, cannot be decided without a study of a larger series of cases.

The usual sequence of events seems to be an initial attack of fever ranging between 99° to 102°F. and persisting for some days or several weeks at a lower range of about 100°F. The lung signs are very transient, sometimes being in evidence only for a day or two. The cough, specially of a dry hacking type, is more persistent. The splenic enlargement and the changes in the x-ray picture of the lung develop more slowly, as also the leucocytosis and eosinophilia in the blood picture. The spleen gradually recedes and the fever disappears. The x-ray appearance of the lung changes from one of scattered small foci to one of fibrosis and heavy hilar shadows. The blood picture remains unchanged or becomes more abnormal, and is probably the last feature to return to normal, sometimes persisting for years.

Case 3 was admitted in October 1939 for cough, slight fever and weakness of 4 months' duration. He had no fever during a stay of 11 weeks in hospital and at the time of discharge, showed clinical improvement and an increase of weight from 98 to 112 pounds. Though keeping quite fit for years, a routine examination of his blood on 14th April, 1944, showed a total W.B.C. count of 15,450 per c.mm. with 59.5 per cent eosinophiles compared to 57.5 per cent in 1939.

The possibility that the initial attack of fever may be absent or slight has also to be kept in mind, the acute condition passing off for a

TABLE I

Case number	I	II	III	IV	V	VI	VII	VIII
Sex and age	M., 29	F., 28	M., 26	F., 45	M., 16	M., 22	M., 7	M., 29
Personal history of allergy	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil
Duration of symptoms till blood examination.	..	8 months	About 1 year	4 months	..	4 months	3 weeks	9 months
Fever	+	+	+	+	+	+	+	+	Nil
Cough	Nil	+	+	Nil	Nil	+	+	Nil	Nil
Lung signs	..	Nil	+	+	Nil	Nil	+	+	Nil	Nil
X-ray changes	..	Nil	+	+	No x-ray	No x-ray	+	+	No x-ray	Nil
Splenic enlargement	..	+	Transient	Marked and persistent.	Nil	Nil	Nil	Nil	Nil	Nil
Hepatic enlargement	..	Nil	Marked and persistent.	Nil	Nil	Nil	Nil	Nil	+	Nil
Total W.B.C. per c.mm.	..	21,300	21,000	15,450	16,000	20,500	23,400	25,100	19,200	..
Eosinophile per cent	..	65.5	36.0	59.5	32.0	61.0	55.0	42.5	67.5	..
Eosinophiles per c.mm.	..	13,951	7,560	9,193	5,120	12,505	12,870	10,667	12,960	..
Blood sedimentation rate : (1 hour and 2 hours readings in mm.).	84-94	38-58	100-108	11-25	27-60	20-45	30-52	..
Wassermann reaction	..	Negative incomplete.	Negative	Positive	Positive	Strong positive.	Strong positive.	..	Weak positive.	..
Kahn test	..	Positive	Negative	Positive	Negative	Negative	Negative	..	Negative	..
Treatment	..	N.A.B. 4 injections.	Acetylarsan 5 injections. N.A.B. 4 injections.	N.A.B. 6 injections.	Acetylarsan 5 injections.	Mapharside 8 injections.	Acetylarsan 10 injections.	Acetylarsan (children's dose) 5 injections.	Nil	..
Clinically	..	Cured	Cured	Cured	Cured	Cured	Cured	Better
Eosinophile per cent after injections.	..	13	12	7	5	12	10

TABLE II

Case number	I	II	III	IV	V	VI	VII	VIII
Millions of R.B.C. per c.mm.	5.35	4.83	6.74	..	5.45	5.44	6.23	5.36
W.B.C. per c.mm.	21,300	21,000	15,450	16,000	20,500	23,400	25,100	19,200
Neutrophils per cent	15.0	42.0	18.0	32.0	11.5	34.0	30.0	20.0
Eosinophiles per cent	65.5	36.0	59.5	32.0	61.0	55.0	42.5	67.5
Basophiles per cent	1.5	1.0	Nil	1.0	1.5	1.0	1.0	0.5
Lymphocytes per cent	16.5	18.0	20.0	30.0	24.0	8.0	25.0	11.0
Monocytes per cent	1.5	3.0	2.5	5.0	2.0	2.0	1.5	1.0
Ova in faeces	Nil	Nil	Hookworm ova present.	Nil	Nil	Nil
Blood group	iv/0	..	i/AB	ii/A	iii/B	..
Coagulation time	3 minutes 40 seconds.	..	4 minutes 30 seconds.	4 minutes 30 seconds.
Fragility of R.B.C. in terms of saline concentration.	..	0.42 per cent to 0.32 per cent	0.44 per cent to 0.28 per cent	0.42 per cent to 0.34 per cent
Blood urea in mg. per cent	49 mg.	28 mg.	..	50 mg. (1941) 25 mg. (1943)
Blood sugar in mg. per cent	86 mg.	112 mg.
Other tests, signs, etc.	..	Gel test : negative. Sputum : <i>B. tuberculosis</i> not found. Heavy reaction with acetylarsan but not with N.A.B. injections.	Admitted in hospital in October 1939. von Pirquet's test and Yoshida's reaction negative. Free from symptoms from 1940 onwards.	Enlarged groin glands of one year's duration.	Blood culture sterile. Widal reaction negative.	Serum calcium 9.5 mg. per cent.	Sternal puncture smears showed 25.5 per cent eosinophiles. Weight increased from 42 to 52 lb. after 5 injections.	Free from symptoms. Recent examination showed R.B.C. 5.37 millions, W.B.C. 21,000, eosinophiles 66 per cent. Sedimentation rate 47.74 mm.

common cold or bronchitis. A routine blood examination only may reveal the condition (e.g. case 8).

Blood changes.—The change in the blood picture in the direction of an increasing leucocytosis with a high eosinophile percentage constitutes the essential diagnostic criterion. The total W.B.C. counts in this series ranged from 15,000 to 25,000 and the eosinophile percentage from 32 to 67.5. The total eosinophile counts are more reliable for comparing cases and assessing the progress in each case than the percentage figures.

These absolute figures varied from 5,120 to 13,951 per c.mm. Still higher figures have been recorded in other reports.

The morphology of the eosinophile cells is normal. Practically no myelocytes and immature cells are seen in the blood smears. On the other hand, the tendency is towards a shift to the right resulting in the appearance of more cells with hypersegmented nuclei. A differential count of 100 cells in one smear showed the following distribution :—

Number of nuclear lobes	1	2	3	4	5
Neutrophiles per cent ..	6	51	35	8	Nil
Eosinophiles per cent ..	1	64	30	5	Nil

In another case, the figures were :—

Eosinophiles per cent ..	3	91	6	Nil	Nil
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The eosinophile cells are thus mainly of the mature type.

The white blood corpuscles other than eosinophiles, though showing lower percentage figures on differential count, remain within normal limits in cells per c.mm.

The red cell count, despite the fever, emaciation and illness, remains practically normal. In fact, the figures in these cases are generally higher than normal, e.g. 5.35, 6.74, 5.45, 6.23 and 5.36 millions. The altitude at Coonoor—about 6,000 feet above mean sea-level—may be responsible for these high figures, but those of the other reports which mention the red cell counts also show a level practically normal.

Other tests carried out on the blood in one or more cases include blood culture, agglutination reaction, coagulation time, estimation of serum calcium, blood urea and blood sugar, fragility of red cells, the gel test and blood grouping. These did not reveal any significant deviations from the normal range. Three cases grouped were found to belong to group i/AB, group ii/A and group iii/B respectively.

Sternal puncture smears were examined in case 7. A differential count on 1,000 nucleated cells gave 6.5 per cent immature and 19 per cent mature eosinophile cells, with a total of 25.5 per cent eosinophiles, the figures in the peripheral blood of this patient being 25,100 W.B.C. per c.mm. with 42.5 per cent eosinophiles, i.e. 10,667 eosinophiles per c.mm. Sternal puncture smears have not been mentioned in other case reports. The normal figures quoted by Whitby and Britton

(1942) and Doan and Zervas (Downey, 1938) are as follows :—

	Whitby and Britton Per cent	Doan and Zervas Per cent
Mature eosinophiles ..	0 to 4	0 to 1
Immature eosinophiles ..	0 to 10	0 to 4.1

The sedimentation rate is increased, and it constitutes a good index of the progress under treatment. The usual figures with the Westergren tube but with oxalate solution as the anti-coagulant are 25 to 50 mm. at the end of one hour as compared to normal upper limits of 10 mm. in males and 15 mm. in females.

Serological changes.—The Wassermann reaction and the Kahn test were both done in seven out of the 8 cases. These results are tabulated below along with the others for comparison, from a series of 100 consecutive cases done in the laboratory, using the same technique for the tests.

Eosinophilia cases			Control cases
1	W.R. —	Kahn —	57
1	W.R. +	Kahn +	13
4	W.R. +	Kahn —	1
Nil	W.R. —	Kahn +	8
1	W.R.	Kahn +	7
	neg. incomp.		
Nil	W.R.	Kahn —	7
	neg. incomp.		
7	Total	93

In none of these cases, was any history available or evidence present to suggest the previous incidence of syphilis. It would thus appear that this syndrome is responsible for false positive reactions, specially in the Wassermann reaction. The combination of a positive Wassermann reaction and a negative Kahn test seen in no less than four out of 7 cases is an unusual finding which merits further attention. In the parallel series, only one blood showed this combination. On enquiry, it was found to be a treated case of syphilis; but the blood picture showed 9 per cent eosinophiles on differential count out of a total W.B.C. count of 7,700, thus making it a possible case of this syndrome treated successfully with arsenic.

The occurrence of false positive reactions in these cases is not a new or unsupported finding. Greval *et al.* (1938) and Greval (1940) suggested the name 'lecithinophile eosinophilia' for such cases giving false positive W.R. reactions, when he reported 2 cases. He attributed this to the affinity of the blood serum for the lecithin in the W.R. antigen. Fridodt-Möller and Barton (1940) commented upon the high percentage of

positive Kahn reactions in their series—15 out of 113—almost double the rate among their run of patients, and noted that there was no evidence of syphilis in any of these cases. Thus, this syndrome is likely to be diagnosed often as tuberculosis from the clinical, as atypical leukæmia from the hæmatological, and as syphilis from the serological, findings alone.

Treatment.—It is beyond doubt that many of these patients get over the acute period of trouble with or without treatment. The blood changes, and to a lesser extent, when present, the x-ray changes, persist when the clinical picture has come back to normal. Arsenical treatment, however, shows its effect on these, also in addition to the clinical improvement of the patient. Various arsenical preparations by several routes have been tried and found useful—thus, mapharside and neoarsphenamine

Typical asthmatic wheezing is present in very few of these cases. The changes shown in the x-ray over long periods are not suggestive of an allergic basis.

The sedimentation rate of the blood is usually definitely accelerated in this syndrome. There have been reports of accelerated sedimentation rate in cases of asthma but no effort has been made in such cases to eliminate the possibility of inflammatory changes. Generally, the sedimentation rate is either unaltered in allergic states or retarded. Cutler (1940) includes allergic states, e.g. asthma and hay fever in the group not influencing sedimentation, while Beck (1938) classifies allergy under the group pathologic decrease of sedimentation rate.

The following figures from the records of the Institute clinical laboratory support these views :—

	Total W.B.C.	Eosinophiles per cent	S.R. (WESTERGREN)	
			1 hour	2 hours
Hay fever	6,850 per c.mm.	14	5 mm.	9 mm.
Bronchial asthma (acute phase) ..	14,000 " "	1	2 mm.	8 mm.
Chronic asthma	8,500 " "	11	5 mm.	18 mm.

intravenously, acetylarsan or sulfarsenol intramuscularly, stovarsol, carbarsone or other preparations orally. Both by the intravenous as well as the intramuscular route, the first one or two injections have been followed by heavy reactions in which the fever, lung signs as well as blood counts have become worse. Even with treatment, the x-ray changes and the blood counts are by far the last to come to normal. The mode of action of arsenic must remain uncertain till the ætiology of the syndrome is clear.

Discussion.—While there is general agreement in regarding it as a clinical entity, its ætiology and relationship to other diseases remain unsettled. Weingarten (*loc. cit.*) on the basis of his series of cases seen mostly in Bombay holds that residence near the sea as an ætiological factor is unquestionable. No other proof has been adduced in favour of this view, and no explanation given as to how this factor acts. In at least one of these 8 cases, the patient has not lived by the sea-side at any time in his life, while 2 others have been near the sea for less than a few months altogether.

The blood picture has been responsible for two other theories of ætiology. Frimodt-Møller and Barton have suggested an allergic origin. Most of the cases in this series on specific questioning have given a negative familial and personal history with regard to asthma, eczema, urticaria and other allergic manifestations. Fever lasting for a period of weeks and splenic enlargement are findings hardly ever seen in allergic conditions. The physical signs in the lung when present are more often fine râles.

The serological reactions also do not favour an allergic basis. Even with regard to the point in favour of it, *viz.* eosinophilia, two facts are often overlooked—(1) that even when eosinophilia is present in allergy, the total leucocyte count is often normal or only slightly increased and the absolute eosinophile count rarely exceeds 2,000 per c.mm. as compared to the figure 5,000 and over per c.mm. seen frequently in this condition; (2) that many cases of asthma, eczema and other such conditions do not show any eosinophilia at all. There is thus only slight evidence in favour of, and quite an appreciable volume, against the allergic theory.

Simeons (*loc. cit.*) terms this condition benign eosinophile leukæmia. There is a superficial resemblance between this condition and leukæmia. The absence of myelocytes and their precursors, and the uniformly good prognosis observed in these cases, are however strong arguments against the condition being one of leukæmia. Moreover, eosinophile leukæmia is not a well-established entity like myeloid and lymphoid leukæmias. Several cases with predominance of eosinophilic cells at one stage have been found at autopsy to be typical myeloblastic leukæmias with complete absence of eosinophilia stem cells, e.g. Thomsen and Plum's case (1939), and this has led some authorities to hold the view that eosinophilia may be only a symptom complex of a particular form of myeloid leukæmia. At least some of the cases recorded under eosinophile leukæmia could very well be examples of this syndrome, e.g. Giffen's case (1919) with hypersegmented

eosinophile cell increase, myelocytes less than one per cent and death due to empyema after pneumonia after an interval of 6 years, McDonald and Shaw's case (1922) with a similar blood picture and recovery after splenectomy, Harrison's case (Downey, 1938) with symptoms resembling those of tuberculosis and Mathew's case in a girl aged 12 with a total W.B.C. count of 12 to 15 thousands and an eosinophile percentage of 85. Richter (Downey, 1938) reviewing these cases concludes: 'whether these cases are really eosinophilic leukaemia or are eosinophile leucocytoses due to undiscovered agents has not been determined'. Thus, the very existence of a condition of eosinophile leukaemia is still under doubt. To postulate the existence of a benign eosinophile leukaemia is therefore only to add to the confusion.

It is but one step from the leucoses to the leukaemoid reactions. We can broadly divide these reactions under two groups—the non-infective and the infective. The former group includes Hodgkin's disease and metastatic malignant deposits, both causing leukaemoid reactions only if and when the deposits irritate the bone marrow. The favourable prognosis in the eosinophilic syndrome rules out these two causes.

We are therefore left with the infective group of such reactions to account for the syndrome. The next question is, what is the infective agent responsible for the reaction? Metazoal infections suggest themselves immediately, e.g. trichinosis, filariasis, ankylostomiasis and other helminthic infestations. There is the condition known as Loeffler's syndrome with an x-ray picture of the lung rather resembling the one in this; but Loeffler's syndrome is a very transient condition and diagnosed purely on mass x-ray examination. Frimodt-Møller and Barton's cases showed a smaller incidence of helminthic infestation than a control group. The absence of anaemia of even slight or moderate severity in these cases, the fact that a complete course of anthelmintic treatment has no effect on the clinical, haematological or x-ray changes, even though the ova disappear from the faeces (e.g. case 5), and the generally negative findings for ova in most of the cases, all are points against a helminthic basis for the syndrome. The degree of leucocytosis and eosinophilia generally found in these cases is very rarely found in the helminthic eosinophilias, with the possible exception of trichinosis. This narrows down our field of choice of the infective agents to the lower groups, viz, protozoa, bacteria, or viruses.

From the clinical standpoint, the theory of an infective organ fits in remarkably well with the findings. The low irregular fever, changes in the lungs, occasional splenomegaly in the febrile period with or without a hepatic and glandular involvement, the natural progress towards recovery even in untreated cases—all are familiar accompaniments of many infections

such as enteric, relapsing and Malta fevers; even the leukaemoid reactions are found in some of the infections. Infectious mononucleosis is a striking example, with a blood picture hardly to be differentiated from monocytic or lymphatic leukaemia, and a favourable prognosis. A further point of similarity between these two conditions is the occurrence of false positive Wassermann reactions in both. Thus, Tidy (Downey, 1938) reports 50 per cent of cases in the 1930 London epidemic of mononucleosis giving positive Wassermann reactions. Whooping cough is another infection causing a marked leucocytosis due to an increase of one cell type, lymphocytes, while scarlet fever is responsible for an eosinophilic increase. The balance of the evidence thus seems to be in favour of regarding this syndrome as the result of an infection, the exact nature of which is still unknown. The striking results obtained by arsenic in treatment lend further support to this view.

Summary

1. An analysis is given of the clinical and laboratory findings in eight cases of the syndrome known as tropical eosinophilia.

2. It is suggested on the strength of these findings and a review of relevant literature on the subject that the syndrome may be the result of an infection, the responsible organism being yet unidentified.

Acknowledgment

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'TROPICAL EOSINOPHILIA'

A REPORT ON FIFTEEN CASES

By H. B. LAL

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IN view of recent reports on this condition, a search was made for the existence of tropical eosinophilia among the patients of this hospital. It would have been an enormous task if every case with a complaint of chest symptoms was subjected to x-ray investigations and blood counts, so a plan was hit upon, which was as follows. It is the routine of this hospital to have a thick smear of blood examined for malarial parasites for each patient; opportunity was taken of finding out if there was a preponderance of eosinophil cells among the white cells. When such a preponderance existed, if the patient complained of lung symptoms, a complete investigation of the case was done, and in a great majority of cases the condition looked for was discovered.

It is believed that the diagnosis and treatment of *eosinophil lung* is now a common-place occurrence, but it is felt that the medical profession is entering into a complacent attitude of accepting the existence of the condition as a separate clinical entity which has a specific treatment, namely arsenicals. My belief that such is not entirely the case, has led me to report briefly on these cases.

Symptomatology.—Among these patients, the main complaint was an irritant cough, which was very persistent and very sensitive to weather, a drop in temperature or increase in humidity due to rainfall being accompanied by an increase of this symptom. The cough furthermore was more troublesome in the night than during the day, so much so that all cases required frequent doses of the hospital linctus to secure sleep. The cough was frequently unproductive or accompanied by very slight expectoration; free expectoration was seen in only six cases, being mostly mucoid.

Very prominent among the symptoms was pain in the chest, more often substernal but frequently a generalized one. It was usually of a dull aching character; a sense of constrict-

tion was complained of by only two patients, while nine complained of pain. Breathlessness on exertion was complained of by six patients, though the amount of exertion required to bring it on varied. It furthermore showed no relationship to the severity of the lung lesions as judged by physical examination or x-ray films.

Difficulty in breathing accompanying the nightly spasms of cough was fairly frequent, but only one patient complained of frank attacks of asthma.

All patients except three remained afebrile; one ran a low type of fever during the earlier part of treatment, and two developed moderately high temperature (101°F.) due to an exacerbation during the course of injections.

Physical signs.—These varied considerably from case to case, and it was concluded, that no case could be diagnosed by physical findings only. Definite consolidation was found in four cases, mostly over the right base. Bronchospasm was a more frequent finding, eleven cases showing harshness and prolongation of the expiratory phase, accompanied by rhonchi of varying pitch. Signs of simple congestion of the lower lobes of the lungs in the form of moist sounds were found in six cases. However, four patients were remarkable in that they showed hardly any physical signs in spite of definite x-ray findings. Signs appeared for the first time in two of these cases after the institution of treatment.

Exacerbation of signs.—Three patients developed exacerbations during their stay in hospital. In two of them, it was accompanied by a sharp rise of temperature. In all three cases there was an exaggeration of pain in the chest, cough and expectoration, accompanied by an even greater increase in the chest signs. (Two cases that developed signs for the first time during treatment are not in addition to these three.) One patient developed pleurisy over the original area of consolidation, and a slight dilatation of the heart, both lasting for about a week. In each case this new development was treated with a course of sulphapyridine with remarkable results as regards the lung condition as well as the blood counts, the latter rapidly changing towards normal.

Duration of the disease.—This varied from one month to 10 years, the majority of the patients giving a history of having had the complaint for the past 2 or 3 months only. Two patients revealed a history of an exactly similar attack two years earlier, both these giving a very short duration of the present attacks. Two cases started with an attack of pneumonia, one 10 years ago. One case started with an injury to the chest 3 years ago, which resulted in expectoration of small quantities of blood for about 5 days. Three cases were prone to yearly winter attacks for a number of years.

Blood eosinophilia.—Since a marked increase of eosinophil cells in the blood counts is in our

opinion the final criterion of the diagnosis of the condition, the following observations are noteworthy :—

1. One of our earlier patients was treated for acute bronchitis and discharged to the convalescent depot. He returned to the hospital after a period of 2 weeks with a full-fledged attack of 'tropical eosinophilia', substantiated by white cell count and x-rays. On his first admission he definitely had an absolutely normal blood picture, but on the second admission he had a leucocytosis of 21,800 with 42 per cent eosinophil cells.

2. An exacerbation of symptoms which occurred in three cases was accompanied by a rise in the eosinophil cell count. This occurred in spite of the treatment having been instituted. It was felt that both occurrences were precipitated by an upper respiratory passage infection, and that the symptoms of rhinitis and pharyngitis were due to the infection, rather than to the exacerbation. In each case, the patient was given the usual doses of sulphapyridine, and both the signs in the lungs and the blood counts responded rapidly, the latter falling to normal or even lower levels.

3. The rise in the eosinophil cell count was accompanied by an almost total disappearance of monocytic cells from the blood, these cells returning again as the condition subsided.

4. Eosinophil cells showed themselves in two forms, one being a small compact cell with highly staining coarse granules tightly packed, and the other large cells with moderately staining granules loosely packed, the latter cells being at times much larger than the accompanying neutrophil cells. The significance of these two types of cells could not be judged in this series.

5. The response to arsenicals was dramatic in each case, and the effect of the drug (novarsenobillon) was equally good on the symptoms, the physical signs and the blood counts. Serial x-rays could not be taken due to shortage of films, but in two cases observed, the lungs were clear of all abnormalities at the second examination. There was usually a rise in the total white cell count and the eosinophil cell count after the first injection, occasionally accompanied by increase in discomfort of the patient as regards cough and pain in the chest. This reaction was however short-lived, seldom lasting more than 36 to 48 hours.

The blood counts and their response to treatment with arsenicals, sulphapyridine, and patient's own blood are charted below*.

X-ray findings.—It was disappointing not to find the classical diffuse mottling spread over the lung fields in all the cases. When present, it was most characteristic, but it was seen in only

five cases. The mottling was of a coarser nature than that of miliary tuberculosis, and could be compared with that of very early pneumoconiosis. However, the size of the individual shadows varied, and they were always more prominent towards the bases. The rest of the cases showed variations from mere congestion of the lungs to a definite patch of pneumonic infiltration. Reticular infiltration of the bronchi was seen in some cases, while thickened pleura was a prominent feature in one. The hilar shadows varied but were mostly increased in size in relation to the pathology in the lung. Again these findings also were more marked towards the bases, and more so on the right than the left side. Enlargement of the right heart was seen in one case already mentioned.

Other investigations.—In this series two cases presented positive blood smears for malarial parasites, both benign tertian, one had a positive Kahn test, and two showed hookworm ova in the stools. There was no definite evidence to indicate a relationship between the eosinophilia and helminthic infection, syphilis or malaria. The sputum was examined for acid-fast bacilli with negative results in all cases. Eosinophil cells were found in the sputum of three cases out of seven in which they were looked for.

Occupation.—The question of the occupation of these patients before entry into the army was studied, and analysis revealed the following categories :—

Farmers	8
Labourers	2
Clerk	1
Student	1
Travelling salesman		..	1
Overseer	1
Moulder	1

There was a marked preponderance of farmers, but then most of the patients in an Indian general hospital are derived from this class. In my opinion, no real significance could be attached to this fact.

Relapses.—In a military hospital it is usually impossible to find the relapse rate in any series of cases, but we got back two patients who had been discharged through the usual channels to a reinforcement camp where they developed a second attack and were readmitted to this hospital in exactly the same condition as previously.

Treatment.—Eleven patients were treated with novarsenobillon; of these nine showed a good result, with the lung condition gradually clearing up, and both the total white cell and eosinophil cell counts diminishing to normality. The other two developed exacerbation of signs and symptoms, and the cell counts rose up in

*This chart showing the records of fifteen patients have been omitted to economize space.

each case, and so were treated with sulphapyridine with dramatic results. One patient was treated with the latter drug only, with similar results. Here it may be mentioned that since the completion of this series, three more patients have been treated with M&B 693 only with excellent results as regards the lung changes and the white cell counts, but these have not been included in this report. Three patients were treated with autohæmotherapy, the results being almost negligible or even detrimental, in spite of the fact that their general condition improved.

Discussion

In this series the following facts stood out boldly:—

1. A history of the disease dating from an infection of the respiratory tract, the patient apparently being left in a sensitive state. In most cases besides the sensitization of the patient, it appeared that the original infection was really never recovered from completely, and that it persisted in a minimal form sufficient to keep up the continuity of the sensitive state. In others, it was the subordinate infection which precipitated the signs and symptoms of 'tropical eosinophilia' (I have used the phrase 'subordinate infection' to indicate a minor infection of the respiratory passages, not severe enough to cause signs and symptoms of its own). This was probably the case in the patient whose first admission was for bronchitis and the second for 'tropical eosinophilia' after a fortnight's stay at the convalescent depot. Among the former cases the original infection persisting in a minimal form may be presumed to have taken on the rôle of the 'subordinate infection'. Two of the cases were obviously extremely prolonged ones. In these any fresh infection just precipitated the effects of the high level of sensitiveness already existing, in the form of exacerbation of the symptoms and signs, and an increase of total eosinophil cells in the blood stream.

2. Variation in symptoms, physical signs and x-ray findings. While the symptoms have varied from mere cough of an irritant nature to periodic attacks of full-fledged asthma, from absence of fever to a rise of temperature up to 101°F., and from a dull pain in the substernal region to a definite sense of constriction and the 'stitch' pain of pleurisy; the physical signs and x-ray findings have varied just as much. The former could be traced from absolute absence of physical findings, through bronchitis, bronchopneumonia to definite massive consolidation and pleurisy. As regards x-ray findings, diffuse mottling similar to that of miliary tuberculosis was definitely the characteristic picture in the larger proportion of cases, but just as frequently the films substantiated the above physical findings.

3. Lack of relationship between the total and differential white cell count and the lesions discovered on physical examination or in x-ray films. The range of the total white cell count was probably controlled by the virulence of the infection and response of the body, rather than the size of the lesion. The total eosinophil cell count seemed to reflect fairly truly the severity of the sensitiveness of the individual. Some cases showed a high eosinophil cell count with a normal figure for total white cells, thereby indicating a moderate degree of sensitiveness existing without any active infection.

The eosinophil cells in the sputum represent the tissue eosinophilia of the bronchial and lung structures, the tissue eosinophilia being the response of the tissues in the presence of a degree of sensitiveness in contrast to a purely purulent reaction. Whether any relation exists between blood eosinophilia and the presence or absence of eosinophil cells in the sputum cannot be gauged.

4. The response of the lung lesions and blood eosinophilia to treatment with sulphapyridine in the acute phases. With the subsidence of the former under this treatment, the total eosinophil cell count fell rapidly to normality, thus indicating that there is a definite relationship of the condition to the existence of bacteria or tissue protein caused by the presence of the offending organism.

5. Lack of permanency of cure with arsenicals and the possibility of exacerbation even during treatment with this type of drug. The exact rôle of arsenic is not understood; it seems to diminish the degree of sensitiveness and so proportionately the eosinophilia, but it does not entirely eliminate either.

The fact that the condition appears at a definite period after an initial infection, which having produced a state of sensitivity, may either subside completely or persist in a minimal form. In the former case the allergic state gradually wanes almost completely; in the latter a high degree of allergy is constantly maintained. In either case it merely requires a subordinate infection to bring about a complete picture of tropical eosinophilia. In the presence of this allergic state, Biggart suggests that the response of the tissue instead of being a polymorphic one, is in the form of eosinophilia; and so also of the bone marrow, there being no essential difference between the tissue and the blood eosinophilia. These both belong to the same category as the eosinophilia of protein digestion, post-febrile eosinophilia, and eosinophilia after repeated protein injections.

The statement made in recent literature that blood eosinophilia was a primary factor and that the lesions in the lungs were due to some precipitating factor, e.g. an infection, could not be substantiated. In the first place one of our cases definitely had no eosinophilia before the attack started, and further three cases responded to sulphapyridine by blood counts returning to normal, which would not have been the case if blood eosinophilia was a permanent factor. Weingarten's suggestion of environment being the controlling factor could not be justifiably commented on, as the area from which these cases were drawn was a very large one, though perhaps uniformly moist; with the exception of the moist and humid climate no special environmental factor could be said to be particularly influential.

Further, it is found difficult to consider it as a new disease entity, though every credit must be submitted to Fridodt-Møller for recognizing its existence and to Weingarten for emphasizing its frequency. Loeffler's syndrome has so far been mentioned as one of the conditions from which tropical eosinophilia has to be differentiated, but I believe that Loeffler was describing the same condition only in children. Holts' description of this syndrome is a masterpiece of completeness in brevity, and it runs thus—'This is characterized by transitory pulmonary infiltrations, which by x-ray present a picture similar to that of miliary tuberculosis, a high degree of eosinophilia is associated. The symptoms are mild with slight fever and cough, occasionally some evidence of pleurisy develops. The course is benign, the condition clearing up spontaneously in a few days or weeks. Little is known as to its aetiology. It is more common in summer months, it is sometimes associated with other evidence of allergy and has been regarded as allergic pneumonia; the eosinophilia may be extreme, often reaching 60 to 70 per cent of leucocytes. The eosinophils show a characteristic alteration, being larger than normal with granules which are usually large but relatively few in number'. It seems obvious from this description that the condition also exists in childhood, and that it has existed in other parts of the world without being recognized. It would seem more proper that the recognition of the condition should emphasize the importance of a more prolonged observation of cases of lung infection as has been realized for sore throats in relation to rheumatic fever. Any occurrence of an eosinophilic response should indicate further confinement to bed and more energetic treatment of the original or the subordinate infection as the case may be. Administration of arsenic in these cases is still empirical; it perhaps merely helps in controlling the degree of sensitivity, but the infection needs other treatment.

Taking all these observations into consideration, it would seem that 'eosinophil lung' is a misnomer, since the condition is not one only of the lung but is accompanied by response on the part of the bone marrow and blood stream as well and also the whole body in general. Perhaps the term 'allergic pneumonia' would be more to the point.

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Indian Medical Gazette

JANUARY

THE FIGHT AGAINST TUBERCULOSIS IN INDIA : A NEW WEAPON NEEDED

THE tuberculosis problem of India is immense. Anti-tuberculosis work has been going on in India for many years and has in recent years been rapidly developing and becoming more highly organized. It is now out of its infancy, and is a lusty and growing child. None, and least of all the present writer, would wish to minimize the importance of the anti-tuberculosis work which has been initiated and is developing under conditions of great difficulty in this country. This work is largely the result of the persistent endeavours of a small number of public spirited persons, some being members of the medical profession, and some not. To them the country owes a great debt of gratitude for their pioneer work and for the fact that some attempt is now being made to get at the facts about tuberculosis in India and to plan and organize anti-tuberculosis work.

The work in India so far has consisted of provision of facilities for diagnosis in general hospitals and in many special clinics, provision for the treatment of a certain number of patients in out-patient clinics, to a limited extent in general hospitals and in tuberculosis sanatoria. The general lines of the work, as far as they go, are those that have been followed in other countries. When however the magnitude of the problem in India is fully realized, two facts stand out. The first is that, on its present lines and present scale, anti-tuberculosis work in India is only a minute fraction of what is needed to begin to make any impression on the tuberculosis problem of India, and the second is that so far practically nothing has been done or attempted in the prevention of tuberculosis in this country. One cannot help feeling that, in the present social and economic condition of India, and even in the improved social and economic condition which is being hoped for and planned for after the war, the control of tuberculosis by present methods in this country will be impossible unless some new factor is brought in to bear on the problem.

Tuberculosis workers themselves are realizing this to an increasing extent. If we glance through the previous tuberculosis numbers of the *Indian Medical Gazette*, we find several articles bearing on this point. In the 1942 tuberculosis number, an article by Benjamin discussed the after histories of treated cases in India and other countries, and quoted the figures of the London County Council indicat-

ing that after treatment only one-third of the patients survived five years. These figures are low, and Benjamin actually records better figures for India, but nevertheless the results of the modern treatment of tuberculosis leaves a great deal to be desired. Artificial pneumothorax treatment does improve the prognosis in many cases but the frequency of its failure is reflected in the large number of cases treated in recent years by the severe and mutilating operation of thoracoplasty. Even with this treatment, the prognosis, though improved, is not very markedly so. We have been informed that in recent years the number of thoracoplasty operations done in Europe has been falling since the limitations of this treatment are becoming widely realized. In the 1942 tuberculosis number, David discussing clinics work in Nagpur and the lack of facilities for isolation quoted the vastly superior resources available for work in England and also quoted the slogan 'Find, Isolate, Educate and Treat'. In India most cases are found late, are not isolated, and with the present resources are not treated; nor are the patients or their families educated. It has been said, and rightly so, that results of treatment will improve with earlier diagnosis, and in other countries much money and effort have been spent in this direction. But in 1943, Trail of Papworth pointed out that between 1927 and 1937 under the London County Council Anti-Tuberculosis Scheme, practically no improvement had appeared in the proportion of early cases admitted to institutions. Is there any reason to believe that a similar campaign in this country will produce any better results?

As a remedy for the failure in early diagnosis, mass miniature radiography of the chest is now being strongly advocated, and an elaborate scheme for this purpose has been set up in England, with provision for free maintenance and care of detected patients in institutions and free maintenance of their dependents during the time they are incapacitated. It is only with adequate social services of the nature envisaged in England that such measures as mass miniature radiography are likely to be widely applicable and to help appreciably in the anti-tuberculosis campaign.

In 1942 Kanga said that, in this country, without isolation, the present anti-tuberculosis measures were creating a false hope and a false sense of security. He advocated the provision of facilities for isolation of tuberculosis cases and their families in towns under careful medical supervision.

In our 1943 number, Benjamin asked the question: 'how much of this widely scattered anti-tuberculosis activity in the various areas is being conducted as part of a well-thought-out plan, and how much it will contribute to the ultimate control and decline of tuberculosis?' He quoted figures from America regarding the organization necessary to control tuberculosis, and considered that there is need for a vast

increase in the number of tuberculosis institutions, which as he states is a very costly programme. In the same number, Shah stressed the urgent need for isolation in India.

In our present number, Benjamin outlines an anti-tuberculosis scheme for an Indian city which involves a vast expansion of anti-tuberculosis agencies.

As will be seen, all tuberculosis workers in India are increasingly realizing the great limitations of the anti-tuberculosis work, and indeed opinion is becoming unanimous that while our present work is of value up to a point, it can never on its present lines and present scale have any major effect on the tuberculosis problem. Moreover, there is increasing unanimity that even if the present resources are tremendously expanded they will still accomplish little towards the control of tuberculosis until the question of prevention of spread of infection is tackled. At the present time, some of the work may only be facilitating the spread of infection, since it gives the patient and relatives a false sense of security and enables them or even encourages them to continue to live with their families and spread the infection for a longer period than they would otherwise do.

The only known methods of value in preventing the spread of infectious diseases are isolation and immunization. Regarding the need for isolation nothing more need be said here. There remains however the question of immunization. Is it possible to immunize against tuberculosis?

This is a question on which at present opinion is divided. The best hope at present appears to lie in BCG vaccine. In 1939 writing in this journal we stated as follows:—

'It seems to me that one great hope for the future lies in the direction of the development of some method of immunizing young people exposed to infection. There is of course the BCG vaccine. Opinions regarding its efficacy are very divided. The development of work on the subject has been greatly handicapped by the terrible tragedy in Germany a few years ago when virulent cultures were accidentally substituted for BCG vaccines, with a high mortality in the vaccinated children. At any rate it is now clear that the vaccine does no harm, and numerous competent workers are convinced of its value. A summary of the findings made in studies of the use of BCG vaccine by Negre and Goyal (1938) has recently been published. It is worthy of note that some large industrial concerns in Europe who recruit Indians for training in Europe and for future work in India, insist on such workers being vaccinated with BCG before going to Europe. If further work demonstrates clearly that BCG vaccine or some modification of it does produce immunity, then I think that there should be a vast field for the application of this measure in India for the immunization of contacts and of workers in industry'.

In the *Indian Medical Gazette* in 1938, a special article by Negre and Goyal outlined the value of BCG vaccine and ended with the following sentence: 'The use of BCG in different countries of the world has shown definitely its efficacy in combating tuberculosis.'

In the May, 1944 issue of this journal we reprinted an editorial from the *British Medical Journal* of December 4, 1943. In this editorial, the meeting of the Tuberculosis Association in London was discussed and the accounts given in London of anti-tuberculosis work in various parts of the world were mentioned. The widespread use of BCG vaccine in Norway was described as follows:—

'Norwegian achievements in the sphere of tuberculosis control are well known: we owe to them recognition of the fact that tuberculin-negative entrants to the nursing profession have a far greater liability to develop tuberculosis in the course of their training than the tuberculin-positive; the voluntary immunization of tuberculin-negative nurses with BCG was begun as long ago as 1926, the vaccine being given subcutaneously and later intradermally. Among the vaccinated the annual incidence of tuberculosis has been 2.6 per cent and the mortality from it 0.2 per cent; the corresponding figures for controls (tuberculin-negative on entry and non-vaccinated) are 17.6 per cent and 1.8 per cent. Tuberculin-negative medical students have been given the same opportunity; the incidence of tuberculosis among the non-vaccinated has been 4.3 per cent and among the vaccinated 1.2 per cent. This effort has been by no means confined to these special classes of person. Although the Lubeck disaster caused an unfortunate and quite unmerited set-back in Norway as elsewhere, BCG vaccination of the general public has been undertaken on an increasing scale since 1935, and the policy in 1940 was to vaccinate the whole tuberculin-negative population, including school children. That the German authorities now in control have stopped this programme will only serve, as Dr. Dedichen said, to increase its popularity when their occupation ceases'.

References are made in this editorial to the use of BCG vaccine on an experimental basis in the United States, in Saskatchewan and among highly susceptible North American Indian population. In New York City, BCG vaccination has been widely used. Lyle Cummins has attempted to use it in England. In many other countries the vaccine has been widely used, and the reports on results appear to have been good. The *British Medical Journal* records that at the Tuberculosis Association meeting in London, a strong feeling was expressed that official inertia in this matter has lasted long enough, and, indeed, resolutions were passed the effect of which will be a request to the Ministry of Health that prophylactic immunization against tuberculosis should be at least countenanced if not encouraged. The editorial goes on: 'to

those familiar with Norwegian work in particular, it may well seem that the experimental period even in man is already over, and that nothing remains but to apply the method at whatever age, on whatever scale, and in whatever classes of person the circumstances demand'. Recently further information has become available to us regarding the use of BCG vaccine. In Soviet Russia BCG vaccination has developed at a great rate. In the *Bulletin of Hygiene*, July 1944, there is the following abstract of an article on anti-tuberculosis work in Moscow:—

'In Tsarist Russia the fight against tuberculosis was largely left to charitable institutions and very little was done. Since 1917 a great advance has been made; many special hospitals and dispensaries have been built, their staffs trained, and a campaign of education of the general public has been carried on. The numbers of patients treated increased rapidly; in 1921 the dispensaries were attended by 7,981 patients, while in 1927 the number had risen to 89,578. The work of the dispensaries had been chiefly diagnostic but from 1928 new methods of prophylaxis and treatment were introduced and BCG vaccine was used in Moscow on a very large scale. Ten newborn infants were vaccinated in 1927, in 1935 there were 2,981 and in 1940 and 1941 every infant was vaccinated. The number of tuberculosis specialists was only 24 in 1917 but in 1939 there were nearly 500.'

'The mortality rate of tuberculosis in Moscow in 1912 was 2.8 per 1,000 of the population; it has now fallen to less than half this figure'.

In the same journal a previous article stated that mass vaccination of the newborn was con-

sidered one of the most important anti-tuberculosis measures in Soviet Russia.

Is it possible that this BCG vaccine, or some modification of it, might be the new weapon against tuberculosis of which this country, India stands in such definite need? We cannot answer this question, but we do feel that the matter should be thoroughly looked into by the Tuberculosis Association of India and that some preliminary studies might be made of the application of this measure on an experimental basis in certain parts of India.

The vaccination of tuberculin-negative nurses or medical students before they undertake hospital work might be taken up. In certain selected areas it might be possible to study the effect of immunization of children living in contact with cases of tuberculosis. Such work might be attempted in certain industrial concerns where the workers are under reasonable supervision and observation for a period of years. These are only general suggestions; more useful suggestions might be made after a careful consideration of this matter.

To sum up the position as we see it; by methods at present being used even if a great development of anti-tuberculosis activity occurs, it will be very difficult, if not impossible, to make any impression on the vast tuberculosis problem of India. For this some method of prophylaxis is essential. At present BCG vaccination seems to be the most promising method. There is every reason why an attempt should be made to study this measure in India to begin with on an experimental basis.

J. L.

Special Article

INDUSTRIALIZATION OF INDIA AND ITS LIKELY EFFECT ON TUBERCULOSIS PROBLEMS

By P. K. SEN, M.B. (Cal.), M.D. (Berlin), Ph.D.,
T.D.D. (Wales)

(From the *Tuberculosis Inquiry, I. R. F. A., All-India
Institute of Hygiene and Public Health, Calcutta*)

In post-war reconstruction of India, industrialization of the country is likely to have an important place. The Bombay Plan has indicated this. The Bhore Committee for Post-War Reconstruction has an independent section on this issue alone. These are some definite and important signs indicating the trend of this country's future development. It is, therefore, time that one should consider what relationship will tuberculosis have with such development. This consideration becomes necessary and significant in the light of the happenings at the rise of industrialization in highly industrialized countries. There, in this period, the tuberculosis

problem became acute, and it took some time before the cause of such an happening could be realized and remedied. During this time, from the beginning of industrial revolution to the realization of the acuteness of the tuberculosis problem, a heavy toll in human life was exacted. It is right that we should learn from the experiences of those pioneer countries, and not repeat the mistakes, but plan the industry in such a way that such toll of life can be prevented or minimized from the beginning.

It may be said that the conditions in our country are different, and therefore the measures of prevention adopted there should not be transplanted in our country. But, I believe, the causes which contributed to increased death rate at the beginning of industrialization in those countries are, for the most part, likely to be the same in this country. It will, therefore, be worth while to recount some of the factors which aggravated the tuberculosis problem in

those countries at the beginning of industrialization.

England, Germany and the United States of America are some of the countries which could be regarded as industrialized to a very great extent. In Great Britain, 68.9 per cent of the male population were gainfully employed in 1931. For Germany the figure in 1933 was 65.7 per cent and for U.S.A. 61.3 per cent in 1930. Among these countries, England was the first to undergo industrial revolution, followed by Germany and then the U.S.A. At the beginning of industrialization, the industrial population of the two first-named countries had to pass through shocking conditions. Authorities of big industrial enterprises mostly cared for the machines and the output of the finished products, and the human element driving these machines was completely neglected. Men and women would live in most filthy conditions and work for long hours amidst the dust and din of the factory. Even young boys and girls were recruited for factory work, and they had to live and work under the same conditions as adults. Trade and industry began with that precious human feeling which constituted the basis of man's entire social progress, that is, to help each other by giving the necessities of life to every individual. But when the industrial revolution came in Europe, this precious feeling was completely pushed to the background. Machines became mightier than man; man's contribution and even his well-being were not thought of. The Germans have rightly depicted this era as 'Siegezug der machine', that is, the period when the machines predominated over everything.

The effect of such an environment on human health was devastating. In the Rhineland, a highly industrialized part of Germany, children of even the age of 6 years were working in the factories from 6 a.m. to 6 p.m. The Prussian military authorities reported to the Central Government at Berlin in 1828 that they could not enlist the necessary number of healthy men from the industrial districts of Rhineland, because of general damage to health as a result of excessive strain, over-work, and the high tuberculosis incidence among the population of these places. In England, the employment of children became very widespread, specially in the cotton mills. The description of the Lancashire cotton mills in 1800 shows how deplorable was the condition there. Hammond (1917), writing on the condition of these factories, says 'they were hot-beds of what was called putrid fever and it was an epidemic at Radcliffe that first drew the public attention to the condition of the apprentices'.

There is no dearth, in the literature, of such descriptions of deplorable conditions. To show the mentality of the machine age and the industrial practices, it will be sufficient to say that even in 1823 a debate took place in the English Parliament concerning the introduction of 20

or 22 shift hours per day. That the health of the workers is irreparably damaged by such practices is beyond doubt, and that the incidence of tuberculosis increases thereby is beyond question.

The following data accepted from Niederland (1940) for the early period of industrialization show that the incidence of tuberculosis remained almost stationary or showed a trend towards rise in the highly industrialized countries of to-day :—

TABLE I

*Comparative tuberculosis mortality in Prussia from 1816-1900 (in period of 5 years)
Death rate per 10,000 population*

Years	Death rates	Years	Death rates
1816-20	29.1	1861-65	27.8
1821-25	26.9	1866-70	20.9
1826-30	29.8	1871-75	29.5
1831-35	31.9	1876-80	27.2
1836-40	29.1	1881-85	27.0
1841-45	27.9	1886-90	25.6
1846-50	30.8	1891-95	24.2
1851-55	30.5	1896-1900	22.3
1856-60	28.2		

Intensive industrialization of Prussia began at the early part of the nineteenth century. Though the records of tuberculosis death rates for a sufficiently long period before the nineteenth century are not available, it is generally known that tuberculosis was on the decline in this period. In this falling curve, the advent of industrialization showed a remarkable effect. The fall stopped and the curve showed a tendency to rise for about 50 years. After this initial effect of industrialization, the rate diminished gradually and definitely. In the case of Prussia, there is a very significant fact. After the war of 1870-71, Bismarck began improving the hygienic and social conditions of the industrial workers, and immediately, from 1871, the death rate began to go down.

The death rates of tuberculosis in England and Wales are not available at the early part of industrialization. The industrial revolution in England began by the end of the eighteenth century. Some descriptions of the industrial population of this period definitely show that disease was rampant among these workers at this period. Conditions here were so much like those in Prussia that there is no reason to think that the reaction to tuberculosis incidence had been different in England and Wales. About 50 years later, that is, when the initial phase of industrialization was over, the death rate began to fall definitely. This period also coincides with the period when definite legislations were introduced for the betterment of the lot of these unhappy workers. Table II will indicate how the incidence of tuberculosis diminished from the year 1861.

TABLE II

Comparative tuberculosis mortality in England and Wales since 1851 (the age standardized death rate of males 1851-60 for pulmonary tuberculosis as 100)

Years	Death rates
1851-60	100
1861-70	97
1871-80	88
1881-90	73
1891-1900	61
1900-1910	50

There is another and more important side of the effect of industrialization on a country's population. After this initial period of increased ill-health, the industrialized countries showed a remarkable improvement in health. Table III* will show the intensity of industrialization of a country in relation to the incidence of tuberculosis :—

morbidity rates. This will be space consuming. It will be adequate, I think, to give the conclusion of the findings of Georg Wolff, who computed all these data and came to the following conclusion.—'However, within the same country as a political and cultural unit, the inhabitants of which partake more equally by law of the general resources of modern civilization, tuberculosis mortality is for the most part lower in agricultural districts and in agricultural occupations than in the industrialized ones, in England as well as in the United States. This is demonstrated by new figures and correlations within the United States, separately for twenty-seven northern, eastern and western states and for sixteen southern states'.

The benefit of wealth acquired by industrial enterprise and trade is not enjoyed by the industrial population alone in a modern state. The agricultural population enjoys this too. The agricultural population is not exposed to the injuries to which the industrial workers are exposed. This is why, comparatively, the latter

TABLE III

Countries in ascending order of agriculture occupation	Census year	PERCENTAGE OF OCCUPIED PERSONS				Death rate from tuberculosis per 100,000 persons 1926-1930
		Agriculture and forestry	Industry and mining	Trade and communication (including hotel service)	Groups 4 and 5 together : index of industrialization	
1	2	3	4	5	6	7
England and Wales	1931	6.4	49.9	27.7	77.6	.94
United States ..	1930	22.0	35.2	27.4	62.6	.79
Germany ..	1933	28.9	40.4	18.4	58.8	.89
Norway ..	1930	35.8	26.5	21.2	47.7	.155
Italy ..	1931	47.3	29.6	12.9	42.5	.127
Spain ..	1920	57.0	24.6	8.1	32.7	.140
Finland ..	1930	64.6	22.0	7.5	29.5	.241

The above table distinctly shows that the more industrialized the country is, the less is the incidence of tuberculosis in it. The reason for such an effect is likely to be this : industry and trade increased the wealth of the nation, and when this wealth was distributed over the country as a whole, everybody got the benefit of it and the general incidence of tuberculosis fell. A question may arise : is this benefit equally distributed over the whole country, that both the industrial and agricultural population derive benefit ? This question can be answered by taking into consideration the incidence of tuberculosis in the industrial and agricultural parts of the same country. Adequate data with regard to this can be obtained from U.S.A., where there are predominantly industrial and agricultural states. Figures can be given from all the states with regard to their industrial and agricultural status and their tuberculosis

population is better off than the former with regard to tuberculosis.

It may be pertinently postulated that this increase, and later decrease, of tuberculosis may not be due to industrialization of a country. Tuberculosis is intimately related to so many social factors that to incriminate one without considering the others may lead to wrong conclusions. But the effect on the tuberculosis curve at the industrial period is so prominent that it is very likely that industrialization had influenced strongly the course of tuberculosis as stated above. That this is likely to be true is shown by Weber (Biraud, 1930) through another experience, the effect during war period. During the last Great War the mortality rate of tuberculosis increased rapidly in the industrial provinces of Prussia and Saxony in Germany, whereas in the agricultural province of Bavaria of the same country the death rate remained almost stationary or showed only a slight tendency to rise. This speaks clearly of

* Made from the data given by Wolff (1940).

one thing only. In modern war, industry has to be speeded up to a tremendous degree, and it can be accepted as a new, though temporary, phase of intensive industrialization of a country. The brunt of this industry falls on the industrial provinces, and tuberculosis death rates rose rapidly and sharply in just these parts. The war brings in its train many other factors, such as malnutrition, stress and strain, etc., and their effect is distributed over the whole population of the countries at war. The agricultural provinces had also to suffer these but not the industrial stresses. The difference in the mortality rates of tuberculosis in these two regions of the country can, therefore, reasonably be accepted as the effect of industry on the disease.

The same effect can be shown in women. During the war, young women were recruited to industry in England, but the older women (over 45 years of age) were exempted. If industry had any special effect on tuberculosis, this will be manifested in the younger women and absent in the older age groups. The following table of comparative mortality from tuberculosis among women in England during the war of 1914-18, according to Collis and Greenwood (1921), shows how the younger age groups were affected. There was no effect on the older age groups.

Year	15-20 yrs.	20-25 yrs.	25-35 yrs.	35-40 yrs.
1913	100	100	100	100
1917	150	131	113	114
1919	130	120	103	94

Looking from these various angles, it seems that industrialization has a definite effect on the tuberculosis incidence of a country. At the initial stage of industrialization, for the first 50 to 70 years, it increases the death rate of tuberculosis, and later, when measures are adopted for the protection of the health of the workers,

When a country is at the threshold of large-scale industrialization, as India probably is, the question is : can this initial toll of tuberculosis be prevented, and general well-being secured from the beginning? It is sure that, if industry is allowed to grow here exactly in the same way as in the above-mentioned countries, the toll of human lives will be very great in India. But we know, through the experiences of other countries, why such toll was taken and also how it may be prevented. If our industrial enterprises are planned, keeping these facts in view, we are certain to prevent or, at least, materially lessen this toll. This will mean a saving of millions of lives.

In such planning it is essential to have knowledge of the incidence of tuberculosis among the industrial workers under already existing labour conditions. Such knowledge can only come through surveys. Surveys should, therefore, be instituted to collect these informations, and the need is urgent and great.

With regard to tuberculosis among the industrial population in India, very little work has been done. Even from what has been done it is evident that there are very high infection and disease rates among them. The death rates of Calcutta, Bombay and Madras, the three fairly industrialized cities of India, are given below from 1931 to 1939 to show what the trend of tuberculosis is in these somewhat stabilized industrial centres. Records after 1939 have not been given, as war conditions supervened, and this will have extra effect on the trend. The mortality figures have been accepted from the corporation reports, and rates deduced in relation to total populations for each year. It is common knowledge that the actual tuberculosis figures will be very much higher, as only a fraction of the tuberculosis cases is reported. However, as all defects are common, this study may provide us with some idea of the course of tuberculosis in relation to time.

Year	CALCUTTA			BOMBAY			MADRAS		
	Number of deaths due to tuberculosis	Estimated population	Rate per 100,000 population	Number of deaths due to tuberculosis	Estimated population	Rate per 100,000 population	Number of deaths due to tuberculosis	Estimated population	Rate per 100,000 population
1931	2,662	1,163,771	194	1,372	1,161,383	118	843	647,230	130
1932	2,280	1,258,283	181	1,232	1,194,233	103	747	660,255	113
1933	2,595	1,352,795	192	1,376	1,227,083	112	855	673,280	127
1934	2,396	1,447,307	166	1,616	1,259,933	128	971	686,305	141
1935	2,856	1,541,819	185	1,697	1,292,783	131	1,032	699,330	148
1936	2,847	1,636,331	174	1,738	1,325,633	131	1,010	712,355	142
1937	3,104	1,730,843	179	1,768	1,358,483	130	1,104	725,380	152
1938	3,021	1,825,355	166	1,794	1,391,333	128	1,193	738,405	161
1939	2,245	1,919,867	153	1,722	1,424,183	121	1,216	751,430	162

and the wealth acquired by industrial enterprises is distributed among the population, this rate falls steadily.

The Calcutta figures show a slight downward trend of the mortality rate. That of Bombay is stationary or slightly on the rise, and that of

Madras is definitely on the rise. These differences in the trends are not surprising, as Madras was the last and Calcutta the first of these centres to be influenced by industrialization. However, these data indicate that even in these centres, the curve is not on the fall but generally on the rise. Such findings should bring home one fact : if on a falling curve such devastations can occur in Europe, how much more will it be here in India where the curve is still on the rise ? We should, therefore, be doubly careful and view this fact with all its seriousness.

With regard to labour conditions, generally, many facts have been noted, specially by the Royal Commission on Labour in India, published by the Government of India in 1931. But there is urgent need for properly planned surveys to bring to light many factors in detail and in proper perspective. A few facts, however, which are likely to have an important bearing on the incidence and spread of tuberculosis in the Indian industrial population, are mentioned below :—

1. *The labour has to be recruited, almost wholly, from rural areas*

As India is not yet industrialized to even a moderate extent, the labour must come from the rural areas which constitute about 90 per cent of the population of the country.

The significance of this with regard to the hazard of tuberculosis is great. The few surveys carried out among the rural and industrial populations of India have shown that in the former the infection rate is low, while in the latter it is very high. In other words, the rural population represents, 'virgin soil'. When people of this type are transferred to a highly tuberculized area, as an industrial area is, they are liable to massive infection and an acute form of the disease. Secondly, it has also been seen that even if a rural person is infected, he can keep that lesion under arrest in his rural environment, but under industrial stresses such a lesion is likely to flare up and produce disease. Important facts of these kinds have been extensively discussed by Professor Cummins (1939), and the hazard was found to be great.

It is, therefore, necessary to take these facts into account while planning. The following methods seem to me to be practicable to minimize this risk under Indian industrial conditions :—

Control of new entrants is the key point

(a) Before a fresh recruit is admitted into an industry he should be tuberculin tested. Those found negative should not be employed in a crowded factory environment. If possible, they should be given jobs outside the factory shed. The reason for this is this : in the factory, crowding and the potential of infection are likely to be high, and these people will run a very great danger of massive infection and consequent disease.

Those who prove positive on tuberculin test may be employed in the factory, but it is wiser

to employ them as apprentices with less strenuous jobs or shorter hours of work for the first three months at least. During this period they might accustom themselves to the changed environment, and therefore the stress and strain will be less and consequently the chance of flaring up of a dormant lesion will be less.

Both the groups, tuberculin positives and negatives, may be employed in the factory work after about six to twelve months of this type of sheltered employment.

(b) All fresh recruits should be housed in the houses or barracks built by the authorities of the industry. It is unnecessary here to discuss the details of housing schemes. This problem is being considered by the Committee formed for this purpose in the Post-War Reconstruction scheme. The special reason for housing these men in such houses is that the crowding can be well controlled by the authorities, and workers may be taken special care of with regard to living with an 'open' case of tuberculosis.

(c) For tuberculin negatives, BCG vaccination may be carried out. Indian industrial recruits may prove to be an important and vast field for use of BCG., and the author thinks that this might effectively minimize the danger to tuberculin-negative new entrants to industry.

2. *Illiteracy and sense of hygiene lacking*

In the villages people live 'in the open', with plenty of sunshine and air around them. Absolute ignorance about rules of health is, to a certain extent, compensated for by such an environment. But in the crowded and insanitary environment of the industrial area, such ignorance may cause untold harm. Such ignorance, with indiscriminate spitting, unhygienic living, etc., can spread tuberculosis very quickly. This factor must be taken into account.

To combat this ignorance, dissemination of knowledge about health is necessary. The spread of knowledge in an ignorant population is extremely difficult, as they cannot understand things in proper perspective unless they have basic general knowledge. It is for this reason that primary education is of great importance even in public health work. It will go a long way if only the masses could be educated to a certain extent. It is for this reason, I feel, that the authorities of the industry should make a special effort to encourage adult education in night schools for the workers.

Though health work is difficult among the ignorant masses, yet in the existing condition, this must be attempted. This attempt must be made with special stress on the new recruits. I believe that the new-comers will take to new ideas and new modes of living much more easily than the workers who had been 'hard-boiled' in the existing ways of life. I do not mean that propaganda for healthful living should be limited to the new recruits; but I stress the point that the new-comers should be taken more in hand than the others. They should have regular

talks on this subject, and the work should not stop there. They should be regularly inspected, supervised and helped to live in hygienic ways. I do not believe that only talk or intensive supervision over a short period will achieve the end. If left to themselves they will certainly revert to old habits and get into other bad habits which are prevalent in an industrial area. The supervision work must be spread over a long period. Once good habits are inculcated among them and made to continue till the old workers have left the industry, such living will be the standard, and subsequent new-comers are likely to follow this without much trouble. Thus, thorough supervision is necessary for over one generation at least. This may be a long period in the life of a man, but it is an insignificant period in the life of a nation. As it is very likely that such supervision will improve and change the unwholesome life of an industrial worker and that this improvement will continue in the next generation, such attempt must be made. The welfare officers may be of great help in this work. I personally believe that such supervision will be possible as the Planning Committee intends to extend and intensify the public health work of the country. Such expansion will be in stages, and it is the intention of this paper to note where the emphasis should lie first, and it is with the new-comers to the industry.

3. Crowding

It is generally known that the industrial areas are notoriously crowded. But such crowding is not caused by the workers only. In jute mill areas in the neighbourhood of Calcutta such crowding is mainly due to outsiders. People from the villages come to the area in search of jobs and stay with their relations or with a man from the same village. I have come across many cases where one worker is given a room in the barrack built by the authority but as many as five or six are living in it; all the others are men of the same village who have come in quest of work. It is obvious that such a practice will cause overcrowding and is bad for health and may cause rapid spread of tuberculosis.

How this could be stopped is a problem. If the authorities are strict, they can stop this in their own houses. But if they stop this, how will they get new recruits and also where will those people live who have come down to a new area? One solution that seems possible to me is building, by the authority, of a few barracks which will be reserved for such people. In accepting this help, the new arrivals will have to be fully under the control of the authority.

In this connection, it must also be stressed that the Government should control the housing or the *bustees* in the neighbourhood. The conditions of these are extremely deplorable, and they are the breeding places of many diseases. Legislation preventing such housing conditions in the neighbourhood of industry is greatly needed.

4. Insecurity of working conditions

The Industrial Board of the Medical Research Council in England has pointed out that of all the causes which undermine the health of the workers, insecurity of the service takes the pride of place. Constant worry regarding what will happen to-morrow can only make these workers unhappy and diminish their resistance against all diseases. Naturally, this may be a predisposing cause of tuberculosis also.

In most industries to-day, a worker is admitted with no guarantee that his services will be continued even if he proves to be a capable worker. It may be argued that this is understood. But a worker cannot be satisfied with this vague security. In fact, my impression is that they do not feel secure at all. I have no doubt that a statistical investigation which should be instituted on this psychological issue will prove the correctness of the above impression. If that were so, then this very important cause of ill-health should be removed. In other words, the terms and conditions of work for a worker should be defined so that the worker will know exactly where he stands with regard to his work.

Workers also remain dissatisfied if they know that they have no say in the matter of these terms and conditions and also no definite way of presenting their grievances to the proper quarters. These may be corrected in many ways, as for example, the formation of Works Councils, etc. It is not pertinent to this paper to discuss these matters. It is only noted that disease and therefore tuberculosis is associated with these conditions, and these should be remedied.

Insecurity at old age is also a factor in undermining the health of the worker, because the thought of the future constantly haunts a man. Old age pensions, etc., should be a factor in lessening ill-health among the workers.

In fact, all social insurance will contribute to the promotion of health of the workers and is likely to diminish the incidence of tuberculosis among the workers. Social welfare and public health work, specially in the industrial community, are inseparable.

5. Insufficient wages

It is not necessary to stress this point as everybody knows that the wages of the workers are simply insufficient for even the minimum standard of life. That tuberculosis will spread if this condition is allowed to persist is obvious.

But another important consideration is necessary in this connection. The meagre wages these workers get are not available to them fully. When a man intending to work in an industry comes to an industrial area first, he is without a job and has no money even for food. He resides with somebody but food has to be bought. This is the time when he borrows rice, etc., from a shopkeeper and lives on that. The condition for such borrowing is that when he

gets a job, he will return the money with interest. The interest is also very heavy, about 1 to 2 annas per rupee per month. This is what is prevalent in the jute mill areas here, and it is likely that something like this is also present in other industrial areas. By the time he gets a job, he is already heavily in debt. When he gets a job on a few rupees a week, he is so much in debt that only the interest comes to about 1½ to 2 rupees per week. He, generally, goes on paying this interest and can never pay off his capital debt. That means that on his rather meagre earnings he has only about one half for himself. This certainly makes his standard of living much lower than he could have utilized the whole of his wages for food, etc.

This, therefore, certainly is a cause which will undermine the health of the workers and make tuberculosis more prevalent.

The remedy of this involves the overhauling of the whole recruitment system for the industrial workers. This has to be reorganized, and the lines along which this should be done cannot be considered in a short paper like this. The Planning Committee should consider this carefully.

Canteens, managed by the authorities and serving cheap, simple and wholesome food, will mitigate, to a great extent, the above-mentioned evils.

In addition to the above-mentioned factors, there are many environmental and other conditions, which undermine the health of the workers and make them prone to tuberculosis, specially at the initial stage of industrialization of a country. There is one outstanding advantage in dealing with the health of the industrial workers. They are, generally, compact communities and are well under the control of the industrial authorities. Public health measures can, therefore, be instituted and followed better. Social welfare schemes can be organized more thoroughly than is possible in the general public or in the civilian population. These advantages are great and should be fully made use of.

Industry, therefore, should not be regarded as harmful for the health of the country, and this is true of tuberculosis also. One point that should be stressed is that we must learn from the experience of others and should not repeat the delay in correcting things which undermine the health in an industrial population. In fact, while organizing industrial enterprise, we should take steps to do away with these factors as much as possible, so that we may not contribute to this heavy toll of life at the beginning but grow a healthy and happy population from the beginning.

Acknowledgment

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Medical News

NATIONAL INSTITUTE OF SCIENCES OF INDIA (Proceedings Vol. X, No. 2, pp. 167-287)

At the ninth general meeting, Sir J. C. Ghosh, President of the Institute, spoke in favour of the establishment of a National Research Council for India. 'The history of the present war has taught us that to neglect research is to invite calamity. . . . The battle of the Atlantic has depended on the courage and skill of sailors and airmen, but it has depended also on the scientists and engineers who devised and used the means of intercepting the U-boats. The fact that in spite of our hardships, the health and good humour of the people in Britain is at least as high as in ordinary times, has depended on vigorous administrative action based on knowledge of nutrition, health and even applied psychology.' Quoting these words from a broadcast of Professor A. V. Hill, Secretary, Royal Society of Medicine, who was himself present at the meeting, the President said that in the past the Government of India had attached little importance to scientific research as an agency for human betterment. Its organization should be considered a vital element of post-war reconstruction. The Council of the Institute had held a symposium on the subject and recommended formation of a National Research Council in order to plan the main lines of scientific work in accordance with national needs, ensure balanced development of all branches of science, etc. The proposal was adopted in the meeting. The proposed Council will consist of scientific and technical experts with a member of the Viceroy's cabinet as President and have four Boards of Research, viz, scientific, agricultural, medical and public health and engineering.

We have also received a copy of the Transactions of the National Institute of Sciences of India, Vol. II, No. 6, pp. 149-192. It includes a study on the finger nails and nail phalanges of twins by S. S. Sarker.

CORRIGENDUM

In the December 1944 number of the *Indian Medical Gazette*, on page 607, second column, after the 31st line, the following words have been omitted: 'its venerable systems, Ayurvedic, Unani and' before the word 'Tibbi' in the 32nd line.

Public Health Section

THE PLANNING OF A TUBERCULOSIS SURVEY TO DETERMINE THE MORBIDITY RATE (WITH SPECIAL REFERENCE TO INDIAN CONDITIONS)

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Introduction

THE Tuberculosis Survey Sub-Committee of the Indian Research Fund Association recommends in their report (1940) the selection of communities or areas for a study of 'infection, resistance, morbidity or mortality' (type II survey) on the results of a preliminary extensive type I survey intended primarily to ascertain the distribution of tuberculosis infection by the tuberculin test. When either by this procedure or for other reasons a community or an area has been selected for a morbidity study, the facilities generally available and the absence of arrangements for miniature skiagraphy render it impossible to include the whole of the selected population for x-ray study. A sample has to be taken. The Survey Sub-Committee has suggested that a representative sample of adequate size should be taken at random, and all of them should be subjected to all the examinations, including skiagraphy. No specific size of the sample has been stated, but the worker has been referred to a statistician for this purpose.

The object of this paper is to offer a guide to the worker in fixing the size of sample. It is common knowledge that cases of active tuberculosis are more frequently found in the groups showing suspicious signs and symptoms and/or a high tuberculin reaction. It, therefore, follows that a judicious utilization of this knowledge may be useful in reducing the number of x-ray examinations required for attaining a desired degree of accuracy in the estimation of the morbidity rate. To investigate this point in what follows it has been assumed that the history will be recorded and the physical examination and the Mantoux test will be carried out as a preliminary to the selection of individuals for x-ray examination. It is not always possible, because of cost, to include the whole population for even this preliminary study. A sample has to be taken, and this sample will also provide the infection rate in the population. How this sample is to be chosen is itself important, and this paper presumes that the sample is selected on the basis of unrestricted random sampling.

To avoid confusion, the preliminary sample chosen will be called the *main sample* and the part of it chosen for radiological examination will be called the *sub-sample*. The population of which the main sample has been taken and of which the infection and disease rates are the objects of the survey will be referred to as the *population*. The paper therefore attempts to work out the extent to which the accuracy of estimation of the morbidity rate is affected by the sizes of the main and sub-samples, and the method of selecting the sub-sample from the main sample.

Basis for the choice of the sub-sampling method

The size of the main and the sub-samples and the methods by which these samples are drawn all affect the confidence with which the incidence of the disease in the population can be estimated from the data made available during the survey. The estimate as obtained from these data cannot exactly coincide with the incidence of the disease in the population. As the number of radiological examinations done and the manner of selecting the individuals for the examination vary, the chance of the sample estimate being near the population value also varies. Our effort should be to recommend that procedure by following which the estimate as obtained from the sample would most frequently be close to the population value. For each procedure, therefore, the range within which the estimate as obtained from the sample can be expected to lie will be first worked out, and the procedure giving the smallest range will be selected as giving the greatest confidence and will be considered as the most accurate.

Sub-sampling methods considered

Four methods of sub-sampling may be considered:—

(1) All suspicious cases as judged from the history and physical examination and all high reactors (3 plus and 4 plus) as judged by the Mantoux test in the main sample, are taken out for x-ray examination. The suspects, using this term to include also the high reactors in the main sample, constitute the sub-sample. None of the unsuspected group is x-rayed.

(2) Not only the suspected individuals in the main sample but also a random sample from the unsuspected group may make up the sub-sample.

(3) A number of individuals may be selected at random from the suspected group and another set from the unsuspected group. The number chosen from each group will be bound down by statistical considerations.

As an extension of this method, the suspected individuals in the main sample may be grouped

into different categories of varying degrees of suspicion according to the information gathered from the history, physical signs and Mantoux test, and a random sample from each group may be taken for *x*-ray study. The unsuspected group will also contribute a certain number of individuals drawn at random.

The simpler procedure where the main sample is divided into only two groups suspected and not suspected will be referred to as sampling method 3.

(4) Without paying any special attention to signs or symptoms or tuberculin reaction, a random sample may be taken out of the main sample, and all the individuals in this sub-sample subjected to *x*-ray examination.

COMPARISON OF SUB-SAMPLING METHODS

General considerations

Before proceeding to consider the accuracy with which these methods of sampling will indicate the true incidence, it is necessary to compare these methods from other points of view. Sampling method (1) is sometimes used with the assumption that all likely tuberculous cases in the main sample will be sieved in into this sample, and the number that may be missed is negligible. This assumption may not be correct, as tuberculosis is notorious for its insidiousness and may remain hidden without any express sign or symptom. It is also quite possible to have such cases in the low tuberculin reactor's group. In a group of 95 such individuals investigated by *x*-ray in a jute mill by Ukil *et al.* (unpublished I. R. F. A. survey), two persons proved to be actively tuberculous. In a group of 76 such individuals investigated by Lal *et al.* (1943) at Barisal, no case was detected. Even accepting the latter experience, there is no reason to think that with larger numbers an incidence rate of $\frac{1}{2}$ per cent cannot be found. This will be all the more true if the history cannot be recorded properly due to illiteracy or non-co-operation of the population surveyed. Therefore, it is seen that the estimate as obtained by sampling method (1) can at best give a *lower limit* for incidence in the population. The upper limit can only be arbitrary. There is another deficiency in this method of sampling. The number of radiological examinations to be made cannot be prescribed definitely before starting the survey, and no approximately accurate budget can be made beforehand.

Sampling method (2) also suffers from the defect that the number of *x*-ray examinations to be made cannot be prescribed beforehand. But as it also includes individuals from the unsuspected group, it will be in a position to provide a range within which the true incidence will lie. Sampling methods (3) and (4) have neither of the handicaps of sampling method (1).

The natural conclusion arising out of this discussion is that sampling method (1) is not suitable at all. Of the other three methods,

method (2) can be advocated only if it gives much greater accuracy than methods (3) and (4). The choice between methods (3) and (4) will rest on the accuracy they give. The study of the accuracy of sampling methods (2), (3) and (4) is the next step.

Statistical considerations

The accuracy of the different methods of sampling can be compared only if we have a fair knowledge of the situations that are likely to arise in practice. A good idea of the proportions of 'suspicious' and 'non-suspicious' cases in the population and of the proportions in each of these groups showing active tuberculosis is essential. Many hypothetical situations can be considered, but the results of a few surveys carried out in India suggest that in practice three broadly defined situations may arise.

A. A population in which 10 per cent belongs to the 'suspicious' group (showing signs or symptoms or a high tuberculin reaction) and 90 per cent to the 'not suspected' group. Five per cent of the persons in the 'suspected' group and $\frac{1}{2}$ per cent in the 'not suspected' group show active disease. Such a situation is likely to arise in rural populations, the incidence of the disease in the population being 0.95 per cent.

B. A population in which 25 per cent belongs to the 'suspicious' group. The disease incidence in the 'suspicious' group is 10 per cent and in the 'not suspected' group $\frac{1}{2}$ per cent. The total incidence in the population works out 2.9 per cent, and this is a likely picture in towns.

C. A population in which 40 per cent belongs to the 'suspicious' group. The incidence of disease in the 'suspicious' group is 10 per cent and in the 'not suspected' group 1 per cent. The incidence of the disease is 4.6 per cent.

This situation is likely to arise in congested parts of cities or in special groups like industrial workers.

Before actually discussing the accuracy of the different methods of sampling, it is necessary to specify how, after sampling, the data obtained will be worked out to provide an estimate of the actual incidence. Here again many methods of estimation may be suggested even for the same method of sampling, and these estimates may differ in their accuracy. Accepted statistical principles recommend only one method of estimation for each type of sampling, and these methods are described in the Appendix. The accuracy of these methods of estimation are the ones of interest. The closeness with which an estimate lies near the actual incidence is given by its standard error, and the formula for obtaining the standard error is also given in the Appendix. The estimate obtained may be higher or lower than the true incidence by twice the standard error. The larger the standard error, the wider is the range and the less accurate is the sampling method.

The magnitude of the standard errors of the estimates depends on :—

(1) The size of the main sample and the way in which it is taken out of the population.

(2) The size of the sub-sample and the nature of the sampling method used for taking out the sub-sample from the main sample.

As explained in the very beginning, this paper is more concerned with item (2) of the above. In order to indicate the most suitable of the three methods of sampling already discussed for taking out the sub-sample, we need only consider the contribution to the standard error of the estimate when sub-samples of the same size are taken out from the main sample by each of these methods of sampling. This contribution has been worked out for various sizes of the sub-sample when the main sample size is 1,000, 2,000 and 4,000, and when the incidence of disease in the main sample satisfies the description A, B and C already given. Table I gives the range within which the estimate as obtained from the sub-sample would lie for different sizes of the sub-sample for each of the three methods of sampling.

The following results emerge from studying the figures in table I :—

(1) The larger the size of the sub-sample the narrower becomes the range for the estimate. This is not surprising as when the sub-sample size becomes the same as the main sample size, the value as obtained from the sub-sample will coincide exactly with that obtained from the main sample and there will, therefore, be no error due to sub-sampling.

(2) Comparing the three methods of sampling, sampling method (4) gives a narrower range than sampling method (2) when the sub-sample size is small, but when the sub-sample size increases the reverse is the case. Sampling method (3) always gives the narrowest range and is to be preferred. When the sub-sample size is large, there may not be much to choose between sampling method (2) and sampling method (3). This only means that, whichever of these methods we use, when the sub-sample size is large almost all the persons in the 'suspicious' group will have to be included in the sub-sample.

Theoretically it would appear that a greater accuracy than is obtained by sampling method (3) may result by subdividing the individuals in the 'suspected' group according to the degree of suspicion, and taking a number of individuals at random from each group, this number being prescribed by statistical theory. The advantage to be gained by the application of this procedure is also of interest. But it is necessary to have an idea of the relative numbers in the main sample falling into the groups of varying degrees of suspicion, and the incidence of disease in each group, before the accuracy can be worked out. The results as obtained in the Jute Mill Survey already referred to was taken as applicable to the main sample. The results obtained in that survey and the manner in which the 'suspicious' cases were grouped for this investigation are indicated in table II. The accuracy was not increased to any appreciable extent by the further subdivision of the 'suspicious' cases. Further subdivision of the 'suspicious' group means more difficulty and the inclusion of more subjective elements without in any way increasing the accuracy for all practical purposes. *Therefore the sampling method (3) is the one to be recommended.*

Sizes of main and sub-samples

In the foregoing section the most suitable method of sub-sampling was suggested, and

incidentally the range within which the sub-sample estimate would lie for different size of the sub-sample was indicated. This range was obtained on the assumption that the main sample had already been chosen. In an actual survey, since errors due to sampling will arise both in taking out the main sample as well as the sub-sample, a range using both these errors is the one of practical interest. On the nature of its variation for different sizes of samples will depend the number of radiological examinations to be made.

The magnitude of error due to the taking of the main sample will depend on the manner in which it is taken. Theoretically this would vary according to whether certain families are chosen at random and all the individuals in the families included in the main sample, or whether individuals themselves are chosen at random. For the purposes of this paper it will be assumed that the latter is the procedure adopted. The former will be the more convenient one for field work. From a practical point of view, however, it is to be expected that the magnitude of error will not be different whichever procedure is adopted.

The size of the main sample no doubt affects the accuracy with which the disease incidence is estimated as it restricts the size of the sub-sample. But the purpose of the main sample is also to estimate the infection rate. Statistical analysis shows that whether the population infection rate is as low as 20 per cent or as high as 80 per cent a random sample of 1,000 or 2,000 individuals subjected to tuberculin test will provide estimates of the incidence with considerable accuracy. As illustrating this point it may be stated that if from a population of 10,000 with an infection rate of 80 per cent, 1,000 individuals are chosen at random, the rate in the main sample will be between 77.6 per cent and 82.4 per cent. With 2,000 individuals the infection rate in the main sample will be between 78.4 per cent and 81.6 per cent. In a population of similar size with an infection rate of only 20 per cent, the sample of 1,000 persons chosen for the main sample will give figures between 17.6 per cent and 22.4 per cent. Thus it appears that there is no need to take more than 2,000 individuals in the main sample if the object is only to estimate the infection rate.

Table III shows the range within which the sub-sample estimate would lie for various sizes of the main and sub-samples taken out of populations of size 10,000 when they follow either of the types A, B and C described previously. The sub-samples are assumed to have been taken out according to sub-sampling method (3). These ranges are approximate, but serve to bring out the changes in accuracy with changes in the size of the sample.

If the original population is less than 10,000, the range will be less than those given in this table. For populations of over 10,000, the ranges will be almost similar to those given in table III.

TABLE I

(a)

Showing the range within which the estimate of the disease incidence in the main sample as obtained from the sub-sample will lie for various sizes of the main and sub-samples and for different methods of sub-sampling

Main sample follows description of population A—disease incidence 0.95 per cent

Size of main sample 1,000					2,000				4,000			
Size of sub-sample as proportion of main sample	Number in the sub-sample	Sub-sampling method (2)	Sub-sampling method (3)	Sub-sampling method (4)	Number in the sub-sample	Sub-sampling method (2)	Sub-sampling method (3)	Sub-sampling method (4)	Number in the sub-sample	Sub-sampling method (2)	Sub-sampling method (3)	Sub-sampling method (4)
0.109	109	0.00-5.16	0.00-2.47	0.00-2.70	218	0.00-3.93	0.00-2.02	0.00-2.19	436	0.00-3.06	0.19-1.71	0.07-1.83
0.118	118	0.00-3.91	0.00-2.40	0.00-2.63	236	0.00-3.04	0.00-1.97	0.00-2.14	472	0.00-2.43	0.23-1.67	0.11-1.79
0.145	145	0.00-2.79	0.00-2.23	0.00-2.44	290	0.00-2.25	0.05-1.85	0.00-2.00	580	0.03-1.87	0.31-1.59	0.21-1.69
0.190	190	0.00-2.22	0.00-2.03	0.00-2.22	380	0.05-1.85	0.19-1.71	0.06-1.84	760	0.32-1.53	0.41-1.49	0.32-1.58
0.280	280	0.10-1.80	0.13-1.77	0.00-1.93	560	0.35-1.55	0.37-1.53	0.25-1.65	1120	0.53-1.37	0.54-1.36	0.16-1.44
0.370	370	0.30-1.60	0.31-1.60	0.15-1.75	740	0.49-1.41	0.49-1.41	0.38-1.52	1480	0.63-1.27	0.63-1.27	0.55-1.35

(b)

Main sample follows description of population B—disease incidence 2.88 per cent

Size of main sample 1,000					2,000				4,000			
Size of sub-sample as proportion of main sample	Number in the sub-sample	Sub-sampling method (2)	Sub-sampling method (3)	Sub-sampling method (4)	Number in the sub-sample	Sub-sampling method (2)	Sub-sampling method (3)	Sub-sampling method (4)	Number in the sub-sample	Sub-sampling method (2)	Sub-sampling method (3)	Sub-sampling method (4)
0.258	258	0.00-6.72	1.65-4.10	1.08-4.67	515	0.16-5.59	2.01-3.74	1.61-4.15	1030	0.95-4.80	2.27-3.49	1.98-3.77
0.265	265	0.00-5.84	1.68-4.07	1.12-4.64	530	0.78-4.97	2.03-3.72	1.63-4.12	1060	1.39-4.36	2.28-3.47	2.00-3.76
0.288	288	1.19-4.56	1.77-3.98	1.21-4.54	575	1.69-4.07	2.09-3.66	1.70-4.05	1150	2.03-3.72	2.32-3.43	2.04-3.71
0.325	325	1.72-4.04	1.89-3.86	1.35-4.40	650	2.06-3.70	2.18-3.57	1.80-3.95	1300	2.30-3.46	2.38-3.37	2.11-3.64
0.400	400	2.10-3.65	2.11-3.64	1.58-4.17	800	2.33-3.42	2.33-3.42	1.96-3.79	1600	2.49-3.26	2.49-3.26	2.23-3.52

(c)

Main sample follows description of population C—disease incidence 4.6 per cent

Size of main sample 1,000					2,000				4,000			
Size of sub-sample as proportion of main sample	Number in the sub-sample	Sub-sampling method (2)	Sub-sampling method (3)	Sub-sampling method (4)	Number in the sub-sample	Sub-sampling method (2)	Sub-sampling method (3)	Sub-sampling method (4)	Number in the sub-sample	Sub-sampling method (2)	Sub-sampling method (3)	Sub-sampling method (4)
0.403	403	0.00-11.48	3.36-5.84	2.99-6.21	806	0.00-9.46	3.73-5.47	3.46-5.74	1612	1.16-8.04	3.98-5.22	3.79-5.41
0.406	406	0.00-9.45	3.37-5.83	3.00-6.20	812	1.17-8.03	3.73-5.47	3.47-5.73	1624	2.17-7.03	3.99-5.21	3.80-5.40
0.430	430	2.47-6.73	3.45-5.75	3.07-6.13	860	3.10-6.10	3.79-5.41	3.52-5.68	1720	3.54-5.66	4.02-5.18	3.84-5.36
0.460	460	3.14-6.06	3.54-5.65	3.17-6.03	920	3.57-5.63	3.85-5.35	3.59-5.61	1840	3.87-5.33	4.07-5.13	3.88-5.32
0.520	520	3.63-5.57	3.70-5.50	3.33-5.87	1040	3.91-5.29	3.96-5.24	3.70-5.50	2080	4.11-5.09	4.15-5.05	3.95-5.24
0.580	580	3.86-5.34	3.86-5.34	3.48-5.72	1160	4.07-5.13	4.08-5.12	3.81-5.39	2320	4.23-4.97	4.23-4.97	4.04-5.16

This table can therefore be used to fix the sizes of the main and sub-samples according to the degree of accuracy required.

In illustration of the use of the table, let us suppose that an estimate of the disease incidence in a rural population is required. Though the incidence will not be known beforehand, it

would be reasonable to assume that it may be somewhat like the population A described before. The disease incidence will be about 0.95 per cent. Table III shows that if a main sample of 1,000 is taken and a sub-sample of 400 out of it is submitted to x-ray examination, the estimate of disease incidence as obtained

TABLE II

Showing the incidence of active tuberculosis in relationship to signs and symptoms and tuberculin reaction (Jute Mill Survey)

Group	Signs and symptoms	Tuberculin reaction	Number of persons examined	Number with active tuberculosis	Percentage with disease
1	Hæmoptysis with cough, fever, wasting and signs of P.T.	High
2	Hæmoptysis with not all the indications in group 1.	Low	24	12	50.0
3	Cough with wasting, fever, signs of P.T.	High	20	10	50.0
4	Cough with not all the indications in group 3.	Low
5	Wasting with fever, signs of P.T. or some other sign.	High	12	3	25.0
6	Wasting with not all the indications in group 5.	Low	6	1	16.7
7	Signs of P.T.	High	1	1	100.0
8	Signs of bronchitis	Low	1	1	100.0
9	All others with some sign or symptom.	High	6	6	100.0
10	No sign or symptom	Low	52	31	59.6
		High	46	23	50.0
		Low	449	30	6.7
		High	351	23	6.6
		Low	219	20	9.1
		High	6	2	33.3
		Low	909	78	8.6
		High	5	1	20.0
		Low but radiologically examined.	6,145	..	0.005 (assumed).
		Low but not radiologically examined.			

Note.—In dividing the 'suspected' group into different categories with varying degrees of suspicion the categories adopted were (a) groups 5 and 6, (b) groups 2 and 7, (c) groups 8, 9 and high reactors in group 10, (d) group 4, (e) low reactors, in group 10.

TABLE III

Showing the range within which the estimate of the disease incidence in the population as obtained from the sub-sample will lie for various sizes of the main and sub-samples from a population of size 10,000

Size of main sample.	Population A—disease incidence 0.95 per cent			Population B—disease incidence 2.88 per cent			Population C—disease incidence 4.6 per cent		
	1,000	2,000	4,000	1,000	2,000	4,000	1,000	2,000	4,000
Size of sub-sample as proportion of main sample.									
0.1	0.00-2.65	0.00-2.14	0.12-1.78	0.33-5.43	1.09-4.66	1.63-4.12	1.02-8.18	2.09-7.11	2.85-6.35
0.2	0.00-2.14	0.12-1.78	0.38-1.52	1.08-4.67	1.63-4.12	2.03-3.73	2.08-7.12	2.84-6.36	3.39-5.81
0.3	0.00-1.92	0.28-1.62	0.50-1.40	1.41-4.34	1.87-3.88	2.20-3.55	2.55-6.65	2.18-6.02	3.64-5.56
0.4	0.12-1.78	0.38-1.52	0.57-1.33	1.61-4.14	2.02-3.74	2.32-3.44	2.83-6.37	3.38-5.82	3.79-5.41
0.5	0.20-1.70	0.44-1.46	0.61-1.29	1.73-4.02	2.10-3.65	2.38-3.37	3.02-6.18	3.53-5.67	3.90-5.30
0.6	0.26-1.64	0.48-1.42	0.65-1.25	1.79-3.96	2.15-3.61	2.42-3.33	3.17-6.03	3.63-5.57	3.98-5.22
0.7	0.30-1.60	0.51-1.39	0.67-1.23	1.82-3.93	2.17-3.58	2.44-3.31	3.25-5.95	3.69-5.51	4.03-5.17
0.8	0.33-1.57	0.53-1.37	0.69-1.21	1.85-3.91	2.19-3.56	2.45-3.30	3.30-5.90	3.73-5.47	4.06-5.14
0.9	0.35-1.55	0.55-1.35	0.70-1.20	1.86-3.89	2.20-3.55	2.46-3.29	3.32-5.88	3.75-5.45	4.08-5.12
1.0	0.37-1.53	0.56-1.34	0.71-1.19	1.87-3.88	2.21-3.54	2.47-3.29	3.34-5.86	3.76-5.44	4.09-5.11

from the sub-sample will be between 0.12 per cent and 1.78 per cent. Such an estimate can certainly not be considered as reasonably accurate. If the sub-sample size is increased to 1,000, i.e. to the size of the main sample itself, the estimate will lie between 0.37 per cent and 1.53 per cent. Even this will not be considered sufficiently accurate. These factors show that though a main sample of 1,000 provided a good estimate of the infection rate, this number will not do for providing a reasonably correct estimate of the disease incidence. Increasing the main sample size to 2,000 and having 1,000 of them examined radiologically increases the accuracy a little, as the range would now lie between 0.44 per cent and 1.46 per cent. If all the 2,000 individuals of the main sample are considered as the sub-sample, the estimate will be between 0.56 per cent and 1.34 per cent, which may be considered as reasonably accurate.

Before prescribing the minimum number of radiological examinations to be made in a population of 10,000, let us examine more closely the advantage gained by increasing the size of the main sample. Table III shows that with a main sample of 4,000 and a sub-sample of 1,600 for x-ray study, the estimate of disease incidence in the rural population will be between 0.57 per cent and 1.33 per cent. This standard of accuracy is even slightly superior to that which was obtained by taking a main sample of 2,000 followed by 2,000 x-ray examinations. Thus it is seen that by increasing the preliminary physical examination and tuberculin testing by 2,000, it is possible to reduce the number of x-ray examinations by 400. This, under the present circumstances in which surveys are carried out, is a definite advantage. The larger main sample has another advantage. If it is desired also to study the epidemiology of infection, the number of individuals examined will have to be subdivided according to factors such as sex, age, habitat, etc., and the larger the size of the main sample, the greater the precision with which such studies could be carried out. From this point of view, an increase in the size of the main sample is to be recommended. It can therefore be concluded that in type II surveys it will be more advantageous to utilize a larger main sample from which individuals will be subsequently selected for x-ray examination.

While discussing the sizes of samples for estimating disease incidence, another consideration presents itself. During the course of anti-tuberculosis work it may be felt that the disease incidence should be estimated at intervals of, say, five years to see if there has been an improvement in the situation. The size of the samples should be large enough not only to give a fair idea of the incidence at any one time, but also to bring out evidence of improvement if really there has been a change for the better. The smaller the size of the samples, the less chance there is of this being achieved.

Considering again the rural population for illustration, let it be assumed that between the two dates the disease incidence has fallen from 0.95 per cent to 0.75 per cent. Suppose that at each of these dates 2,000 individuals are chosen for the main sample and that all of them are examined radiologically to provide an estimate of the disease incidence. Statistical analysis shows that in 23 per cent of surveys the estimate obtained at the second date will be even greater than that obtained at the first date. In only 10 per cent of surveys will statistical analysis by the usual method lead to the conclusion that there is evidence of improvement. So with the sampling scheme involving 2,000 radiological examinations, only in a small proportion of surveys will the sample establish an improvement even if the actual reduction of disease incidence is from 0.95 per cent to 0.75 per cent. It is therefore obvious that as a guide to the improvement effected, even this size of sample is very inadequate. Also increasing the number of radiological examinations beyond this number will not ordinarily be possible. Studies of mortality statistics and their trends at present provide the only indication of a fall in the incidence of the disease; but the accuracy of statistics now available is very doubtful.

To sum up, 2,000 radiological examinations can be expected to give a fair picture of the disease incidence in a population of 10,000 or more. Diminishing the number of x-ray examinations below this number is not encouraged unless it is associated with an increase in the size of the main sample.

RECOMMENDATIONS FOR SAMPLING

Sizes of main and sub-samples

For a population of 10,000 individuals, a random sample of 1,000 or better 2,000, can be considered quite adequate for a study of the infection rate, and it is not advisable to increase the size of the sample unless it is to investigate the epidemiology of infection also.

To fix the size of sample to estimate the disease incidence, table III should be consulted, and the main and sub-sample sizes should be decided upon according to the accuracy desired. The following discussion may be of assistance.

A main sample of 1,000 individuals only, even if all of them are submitted to radiological examination, cannot be considered as yielding a reasonable degree of accuracy; since when the disease incidence in the population is 0.95 per cent, the sample may give an estimate as low as 0.37 per cent or as high as 1.53 per cent, and when the incidence in the population is 2.88 per cent the sample may give values as low as 1.87 per cent or as high as 3.88 per cent.

A main sample of 2,000 persons, all of whom will also be radiologically examined, can certainly be considered as yielding reasonable accuracy. From this procedure when the population disease incidence is 0.95 per cent, the estimate as

obtained from the sample will not be less than 0.56 per cent nor greater than 1.34 per cent. In a population with a disease incidence of 2.88 per cent, the estimate from the sample will lie between 2.21 per cent and 3.54 per cent.

It is hardly possible in many surveys to afford more than 2,000 radiological examinations, but as the examination for infection is not so expensive, it may be easier to take a larger size for studying infection. This will give more accurate figures for the disease rate, and may make the study of epidemiology of infection possible.

Therefore, even surveys which can afford 1,000 radiological examinations in a population of 10,000 cannot be expected to estimate the disease incidence with a fair degree of accuracy, especially when the disease incidence is as low as 1 per cent. *Therefore surveys with facilities for 500 or 600 x-ray examinations only should not be encouraged.*

Two thousand x-ray examinations will be able to provide a degree of accuracy sufficient for all practical purposes. Two procedures may be followed: (1) the main sample may also consist of only 2,000 individuals and all of them are subjected to x-ray examination, or (2) the main sample may be larger, say 4,000, and out of this only 2,000 are selected by sub-sampling method (3) for x-ray examination. The latter method will give more accuracy.

Sub-sampling method

The way in which the sub-sample for radiological examination is to be taken out of the main sample when the former is smaller has been discussed in detail already. Generally speaking, the main sample has to be divided into two groups: (1) 'suspected' (individuals with suspicious signs and/or symptoms, and/or high reactors to tuberculin) and (2) 'not suspected' (the rest), and from each of these groups individuals should be selected at random to make up the sub-sample. The contribution which each of these groups should make is indicated by formula (7) in the Appendix. The formula makes use of the disease rates in the 'suspected' and 'not suspected' groups which as a matter of fact will not be known prior to the survey. But for general application the descriptions of the incidence of disease in rural, urban and selective populations with high disease rate, described previously as A, B and C respectively, may be made the basis for planning. A preliminary sample from the population to be surveyed may also be used to provide the necessary estimates. However, in view of the facilities commonly available, it is our object to make the survey procedure as simple as possible but consistent with a fair amount of accuracy. Therefore, this alternative procedure will not be considered.

The following are the recommendations for the numbers to be selected from the 'suspected' and 'not suspected' groups in the main sample.

If from 100 individuals of the 'not suspected' group in a rural population, a certain number say 'a' is taken for radiological examination then from every 100 individuals in the 'suspected' group three times that number, i.e. 3a is to be taken. For an urban population every 100 individuals of the 'suspected' group should contribute 4.25 times the number contributed by 100 individuals of the 'not suspected' group. In populations with very high incidence of disease, i.e. 4 per cent or over, the numbers to be chosen from 100 individuals of the 'suspected' and 'not suspected' groups will be in the ratio of 3 : 1. The number 'a' will be determined by the total number of x-ray examinations decided upon for the survey.

As illustrating the above rules let us consider the case when a main sample of 4,000 individuals has been taken out of an urban population and 1,000 of them belong to the 'suspected' group and the other 3,000 to the 'not suspected' group. For every hundred individuals of the 'not suspected' group a number 'a' is to be taken. Therefore, the 'not suspected' will contribute 30a. The 1,000 suspected will contribute 42.5a. On this basis, the total number of individuals to be selected for x-ray examination is $30.0a + 42.5a = 72.5a$. If it had been previously settled that 1,500 x-ray examinations can be made then

$$72.5a = 1,500 \text{ or } a = 20.7.$$

Therefore, the number to be taken from the 'suspected' group is $20.7 \times 42.5 = 879$ and that from the 'not suspected' group is $20.7 \times 30.0 = 621$.

In many cases, when the above recommendations are actually applied, it may happen that the number of individuals to be taken out from the 'suspected' group as advised by these recommendations is greater than that actually present in the 'suspected' group. In such circumstances, all the 'suspects' are to be included in the x-ray study and the individuals for the remaining number of x-rays to be made are to be taken out of the 'not suspected' group.

It is no doubt advisable that in every case the above recommendations should be applied to the main sample to decide whether or not all the individuals in the 'suspected' group should be chosen for the sub-sample. But as a general rule it may be stated that if the number of individuals in the sub-sample exceeds 4/10 of the number in the main sample in the case of the rural and urban populations, and 6/10 of the main sample in the case of populations having a disease incidence above 4 per cent, it may be found necessary to include all the suspected persons in the main sample for x-ray examinations.

Estimation of disease incidence in the population

The formula for estimating the incidence of disease in the population is given by equation (9) in the Appendix. The formula for estimating the standard error of the estimate is given either by equations (18) or (19) in the Appendix according as to whether all the 'suspected' individuals in the main sample have been included in the sub-sample or not. The method to work out a range which in all probability will cover the value of the proportion of diseased individuals in the populations is also indicated in the Appendix.

Summary

It is essential that a survey should be planned and a budget made before undertaking it. In such planning, x-ray examination of individuals for determining the morbidity rate is an important and expensive item. Generally the whole population cannot be x-rayed, because of cost. A basis on which to determine the number of individuals to be x-rayed in order to estimate the disease rate in the population with a fair amount of accuracy is, therefore, also essential. This paper aims at providing this basis.

The accuracy with which an estimate as obtained from a sample will reflect the true incidence depends not only on the number of radiological examinations done but also on the manner in which the individuals have been selected for the purpose. Several such methods of selection have been considered in this paper, and the one giving the greatest accuracy is indicated.

It is customary to study infection and disease rates together, and the size of samples to be taken should be such as to provide reliable estimates for both. It is found that while the infection rate can be determined with a fair amount of accuracy even if only 1,000 individuals are selected at random from the population for examination, for estimation of disease incidence a far larger main sample is needed.

For the study of the disease rate it is suggested that from this large main sample, a small sub-sample be selected for radiological examination. The sub-sampling method which is easy to apply and at the same time gives a high degree of accuracy is to divide the individuals in the main sample into two groups, 'suspected' (with suspicious history and/or signs and symptoms and/or high tuberculin reaction) and 'not suspected', and to select individuals from each of these groups at random for radiological examination. The numbers to be selected from each of these groups will vary according to the nature of the disease incidence in the population. As a practical guide three kinds of populations representing conditions of rural, urban, and very high disease rates have been considered, and the rules for making up the sub-sample for each of these populations have been indicated.

Even if this procedure is followed, 2,000 x-ray examinations can be considered to yield only fairly accurate results. With a smaller number than this, the result will be less accurate, and surveys with only 500 or 600 x-ray examinations cannot be recommended especially in populations with low disease incidence. It will, therefore, be noted that a greater number of individuals must be included for the estimation of morbidity rate than is necessary for determining the infection rate. As tuberculin testing and physical examination do not cost much, it is advocated that the main sample for infection study should be increased in size so as to provide

an adequate number of individuals for radiological examination. This will also have the added advantage of making a study of the epidemiology of infection possible.

In a survey of a population of 10,000 or more, it is advocated that the sample for infection study should be about 4,000, and from the latter about 2,000 should be selected for x-ray study according to the following procedure.

The individuals in the main sample should be divided into two groups: 'suspected' and 'not suspected' according to the findings of physical examination and tuberculin testing, and from each of these groups individuals should be taken at random for radiological examination. The numbers contributed by these groups will be such that in a rural population whatever number is selected from 100 'not suspected' 3 times that number should be selected from 100 'suspects', i.e. for the same number of individuals in both the groups the proportion of the contribution of 'suspects' to 'not suspects' will be 3 : 1. This proportion for urban population will be 4.25 : 1 and for populations with very high disease rates (above 4 per cent) 3 : 1.

In cases where the application of the above rules lead to the anomalous position when the number of individuals to be taken from the 'suspected' group is greater than that actually present, all the individuals in the 'suspected' group should be taken and the 'not suspected' group made to contribute the rest.

Formulae for estimating the disease incidence in the population is given in the Appendix.

Acknowledgment

We are grateful to Dr. A. C. Ukil for permitting us to use the data of the Jute Mill Survey, and to Dr. R. B. Lal for his suggestion to introduce this paper in its relationship to the recommendations of the Tuberculosis Survey Sub-Committee of the Indian Research Fund Association.

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APPENDIX

(A) Formulae for estimating the incidence of disease in the main sample and for working out the standard error of the estimate for three methods of sub-sampling.

(a) *Sub-sampling method* (2).—Let M_1 be the number of 'suspected' individuals in the main sample and M_2 the number of 'not suspected' individuals. Let p_1 be the proportion of individuals showing disease in the 'suspected' group and p_2 the corresponding proportion in the 'not suspected' group. The proportion of diseased persons in the main sample p (say) is given by

$$p = \frac{M_1 p_1 + M_2 p_2}{M_1 + M_2} \quad \dots \quad (1)$$

As all the M_1 individuals in the 'suspected' group are included in the sub-sample, all the $M_1 p_1$ diseased individuals in this group will be detected. Of the 'unsuspected' group if m is the number chosen for radiological examination and p_2 is the proportion out of this number showing disease, the proportion of

diseased persons in the main sample is estimated by the formula

$$\text{Estimate of } p = \frac{M_1 p_1 + M_2 p_2}{M_1 + M_2} \quad \dots \quad (2)$$

The standard error of this estimate is given by the equation :

Standard error =

$$\frac{M_2}{M_1 + M_2} \sqrt{\frac{M_2 - m}{m(M_2 - 1)} p_2 (1 - p_2)} \quad \dots \quad (3)$$

(b) *Sub-sampling method (3).*—As in Section (a) let M_1 and M_2 denote the number of individuals in the main sample 'suspected' and 'not suspected' of disease and p_1 and p_2 the proportions in the two groups showing disease. The proportion of diseased persons in the main sample is p (say).

If m_1 is the number taken out from the 'suspected' group for x-ray examination and m_2 the number from the 'not suspected' group and p_{10} and p_{20} be respectively the proportions amongst them showing disease, an estimate for the proportion of individuals in the main sample showing disease is given by the equation.

$$\text{Estimate of } p = \frac{M_1 p_{10} + M_2 p_{20}}{M_1 + M_2} \quad \dots \quad (4)$$

The standard error for this estimate is given by the equation :

Standard error =

$$\sqrt{\frac{2}{\sum_{i=1}^2 (p_i (1 - p_i) M_i^2 (M_i - m_i))}} \quad \dots \quad (5)$$

$$M_0^2 (\bar{M}_i - 1) m_i$$

$$\text{where } M_0 = M_1 + M_2 \quad \dots \quad (6)$$

and Σ shows summation over the two groups 'suspected' and 'not suspected'

If m_0 is fixed as the size of the sub-sample, the minimum value of the standard error is obtained when

$$m_0 \times M_i / p_i (1 - p_i) \times \sqrt{\frac{M_i}{M_i - 1}} \\ m_i = \frac{2}{\sum_{i=1}^2 M_i \sqrt{p_i (1 - p_i)}} \sqrt{\frac{M_i}{M_i - 1}} \quad \dots \quad (7)$$

and in considering this method of sub-sampling in the text it is assumed that the sub-sample has been chosen according to the formula so as to minimize the standard error. This method of sub-sampling has been discussed by Neyman (1934).

In applying the formula given by (7) it may happen that for some values of m_0 the value of m_i becomes greater than M_i . In such cases all the individuals M_i should be included in the sub-sample.

When the 'suspected group' is subdivided into further smaller groups with varying degrees of suspicion and individuals are taken at random from each of these groups to make up the sub-sample, the corresponding formulae are exactly similar to the ones given above.

(c) *Sub-sampling method (4).*—In this method no grouping of 'suspicious' and 'not suspicious' persons is made and the individuals to be x-rayed or selected are at random from all the persons available in the main sample. Let m_0 be the size of the sub-sample and M_0 that of the main sample.

The proportion of diseased persons in the sub-sample will give an estimate of the proportion of diseased persons in the main sample. The standard error of this estimate is given by

$$\sqrt{\frac{p(1-p)(M_0 - m_0)}{(M_0 - 1)m_0}}$$

where p is the proportion of diseased persons in the main sample.

(B) Standard Error for the estimate of the incidence of disease in the population when the main sample is taken at random from the population and the sub-sample is taken by sub-sampling method (3).

Let N be the number of individuals in the population and P the proportion out of them showing active disease. Let M be the size of the main sample made up of M_1 individuals belonging to the 'suspected' group and M_2 individuals belonging to the 'not suspected' group. Assume that p_1 and p_2 give the proportions of diseased individuals in these 'suspected' and 'not suspected' groups and define p by the equation

$$p = \frac{M_1 p_1 + M_2 p_2}{M_1 + M_2} \quad \dots \quad (8)$$

The sub-sample will consist of m_1 and m_2 individuals taken randomly out of M_1 and M_2 respectively, the values of m_1 and m_2 being given by (7). In actual practice the values of p_1 and p_2 will not be known and the formula given by (7) cannot be directly applied. However, for purpose of this theoretical discussion it will be assumed that the values of p_1 and p_2 are known and that the sub-sampling has been done according to the method suggested by (7). If p_{10} and p_{20} be the proportions out of m_1 and m_2 showing disease the estimate of p will be given by p_0 where

$$p_0 = \frac{M_1 p_{10} + M_2 p_{20}}{M_1 + M_2} \quad \dots \quad (9)$$

The expectation of p_0 for fixed values of M_1, M_2, p_1, p_2 , is p and for repeated main sampling is given by P .

The square of the standard error of $p_0, K^2 p_0$ (say) is given by

$$\sum_{p_0} P p_0 (P - p_0)^2 \quad \text{where } P p_0 \text{ denotes the}$$

probability of obtaining the value p_0 from the sub-sample. This expression can also be put equal to

$$\sum_{M_1, M_2, p_1, p_2} P (M_1 M_2 p_1 p_2) \sum_{p_0} P (p_0 / M_1 M_2 p_1 p_2) (p_0 - P)^2 \quad \dots \quad (10)$$

where $P (M_1 M_2 p_1 p_2)$ gives the probability of obtaining the values of M_1, M_2, p_1 and p_2 in the main sample and $P (p_0 / M_1 M_2 p_1 p_2)$ gives the relative probability of obtaining p_0 for given values of M_1, M_2, p_1, p_2 .

$$\therefore K^2 p_0 = \sum_{M_1, M_2, p_1, p_2} P (M_1 M_2 p_1 p_2) \sum_{p_0} P (p_0 / M_1 M_2 p_1 p_2) (p_0 - P)^2 \quad (11)$$

$$= \sum_{M_1, M_2, p_1, p_2} P (M_1 M_2 p_1 p_2) \sum_{p_0} P (p_0 / M_1 M_2 p_1 p_2) (p_0 - p + p - P)^2 \quad \dots \quad (12)$$

$$\sum_{M_1, M_2, p_1, p_2} P (M_1 M_2 p_1 p_2) \sum_{p_0} P (p_0 / M_1 M_2 p_1 p_2) \{ (p_0 - p)^2 + (p - P)^2 \} \quad (13)$$

$$= \sum_{M_1, M_2, p_1, p_2} P (M_1 M_2 p_1 p_2) (p - P)^2 + \sum_{M_1, M_2, p_1, p_2} P (M_1 M_2 p_1 p_2) K^2 (p_0 / p) \quad (14)$$

where

$$K^2 (p_0 / p) = \sum_{i=1}^2 \frac{M_i^2 (M_i - m_i) p_i (1 - p_i)}{M_i^2 (M_i - 1) m_i} \quad (15)$$

using the result given already in equation (5). Also

$$\sum_{M_1, M_2, p_1, p_2} P (M_1 M_2 p_1 p_2) (p - P)^2 = \frac{P(1-P)(N-M)}{(N-1)M} \quad (16)$$



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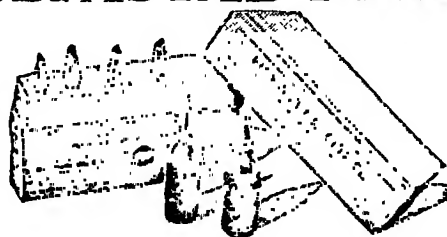
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using the result given in equation (5).

$$\therefore K^2 po = \frac{P(1-P)(N-M)}{(N-1)M} + \sum_{M_1, M_2, p_1, p_2} P(M_1, M_2, p_1, p_2) K^2(po/p) \quad (17)$$

The evaluation of $K^2 po$ requires summation over a large number of terms but it is to be expected that a good approximation to its actual value will be provided by using instead of

$$\sum_{M_1, M_2, p_1, p_2} P(M_1, M_2, p_1, p_2) K^2(po/p)$$

the value of $K^2(po/p)$ for the

particular case where M_1 and M_2 are such that they are in the same proportion as the 'suspected' and 'not suspected' groups in the population and p_1 and p_2 have exactly the same values as the proportion of diseased individuals among the 'suspected' and 'not suspected' individuals in the population. The ranges in Table III have been worked out adopting this approximation.

In an actual survey where the number of 'suspected' and 'not suspected' individuals included in the sub-sample are less than the corresponding numbers in the main sample, the formula to be used will be

$$K^2 po = \frac{po(1-po)(N-M)}{(N-1)M} + \sum_{i=1}^2 \frac{Mi^2(Mi-mi)pio(1-pio)}{M^2(Mi-1)mi} \quad (18)$$

In case all the suspected individuals in the main sample have been included in the sub-sample the formula will be given by

$$K^2 po = \frac{po(1-po)(N-M)}{(N-1)M} + \frac{M_2}{M_1 + M_2} \cdot \frac{(M_2 - m_2)}{m_2(M_2 - 1)} p_{20}(1 - p_{20}) \quad (19)$$

A range which for all practical purposes will cover the value of the proportion of diseased individuals in the population is obtained by working out its extreme values by adding to or subtracting from its estimated value po twice the value of $K po$ as given by (18) or (19) as the case may be.

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Current Topics

Chemotherapy in Tuberculosis

(From the *Lancet*, ii, 8th July, 1944, p. 50)

THE search for a drug more lethal to the tubercle bacillus than to its host still goes on. Rich and Follis first called attention to the inhibitory action of sulphanilamide on the tuberculous process in guinea-pigs if—and only if—the treatment was begun simultaneously with the infection, and only if the drug was administered in highly toxic dosage. Of their treated animals, 60 per cent died within the experimental period of 5-6 weeks. Sulphathiazole was found by Ballon and Guernon to exert a pronounced bacteriostatic effect on virulent human tubercle bacilli on solid media, and to inhibit the development of experimental tuberculosis in the guinea-pig; but 7 of their 42 treated animals died, not of tuberculosis but presumably of sulphathiazole poisoning. Zucker, Pinner and Hyman treated 13 patients with sulphanilamide by the intravenous-drip method, maintaining the blood levels between 17 and 32 mg. per 100 c.cm. for five successive days at a time. All their patients showed headache, cyanosis, mental depression, dyspnoea, fever and temporary drop in haemoglobin, and in no case was the

improvement in their tuberculosis greater than could have been expected on bed-rest alone.

The discovery of Buttle and his colleagues that 4:4'-diaminodiphenylsulphone was much more powerfully bactericidal for streptococci than sulphanilamide directed attention to the effect of this, and of derived 'sulphones', on the tubercle bacillus. In an experiment that lasted 228 days, Feldman, Hinshaw and Moses found this drug, too, to be of the kill-or-cure variety. By the end of the period 71 per cent of their untreated control animals had died of advanced tuberculosis, and the same proportion of the treated group were still alive and flourishing. These animals, when killed, showed small discrete foci and every evidence of retrograde process. Nevertheless 29 per cent of the treated group died, presumably from the toxic action of the drug. Promin (sodium p,p'-diaminodiphenylsulphone-N,N'-didextrose sulphonate), the first derivative of this parent substance, although far inferior in its bacteriostatic action on tubercle bacilli *in vitro*, has been found by Feldman and his colleagues to modify progression and favour healing of tuberculosis in the guinea-pig with a far smaller drug-toxic mortality. Their experiment was repeated by Steenken, Heise and Wolinsky, who in addition treated a group of guinea-pigs inoculated 3 weeks before with living attenuated bacilli (H. 37 'Ra'), thus making the experimental conditions somewhat more comparable with those in clinical human tuberculosis. In this vaccinated group promin had more inhibitory effect on the progress of the subsequent virulent infection than it had in the unvaccinated group. Promin has been administered by mouth and intravenously, and in large concentration maintained by intravenous drip, but the results have not so far been encouraging. Direct local application to tuberculous larynxes, sinuses, pleural effusions and ascites have shown much more promising results.

The latest sulphone derivative, promizole (4:2'-diaminodiphenyl-5'-thiazole-sulphone) has recently been described by Feldman, Hinshaw, and Mann. In their experiments administration of the drug was delayed for 6-14 weeks after the animals had been inoculated with virulent human bacilli; 226 days after inoculation 80 per cent of the control animals had died of tuberculosis, but 90 per cent of those whose promizole treatment had been started 6 weeks after inoculation were still alive. Of a group whose treatment had been delayed 14 weeks, 67 per cent survived. Here, then, seems to be a drug well tolerated by guinea-pigs over a long period, effective in dosage about half that of promin, and exerting a favourable influence even when its administration is delayed long enough to allow the disease to gain a firm hold. Promizole appears to be even better tolerated by man; during the past year it has been administered with impunity to 56 patients in dosage sufficiently large to produce blood concentrations comparable with those attained in the guinea-pigs; only slight and transient toxic reactions were noted. No evaluation of the clinical results in these 56 cases has so far been attempted—it will be months before the effect of the drug, if any, on the progress of the disease can be assessed.

The ideal cases of tuberculosis for chemotherapy are those where invasion has been fairly recent and the disease is infiltrative, rather than those showing acute focal reactions with necrosis, liquefaction and excavation. In the former type successful chemotherapy might mean complete resolution; in the latter, fibrosis and bronchiectasis are still likely to challenge the surgeon. Promizole or its successors may furnish one answer to that vexing question, 'How are we to treat the flood of subclinical cases revealed by mass radiography?'

Diasone in Tuberculosis

(From the *Lancet*, ii, 29th July, 1944, p. 151)

SINCE their curiosity was whetted in March by revelations in the lay press, tuberculous patients and their friends and relations have had nearly four months

in which to bombard their medical advisers with questions about diasone, from which the medical advisers have had up to now to take evasive action. Now, at long last, an authoritative account of the clinical experiment under discussion has reached this country. Diasone is the disodium formaldehyde sulphoxylate derivative of 4:4'-diaminodiphenylsulphone, and thus is sib to promizole accounts of which were reviewed in the *Lancet* of 8th July (p. 50). First synthesized in the United States by G. W. Raiziss and by Bauer and Rosenthal in 1938, its effect on the tuberculous guinea-pig has since been thoroughly investigated by Callomon and Feldman, Hinshaw and Moses, who found that although it was somewhat less lethal to the tubercle bacillus than the other sulphones it was also less lethal to the treated animals. Petter and Prenzlau have now reported on the response of 44 patients suffering from pulmonary tuberculosis who had courses of diasone therapy lasting 120 days or more in 1943. These cases were unselected, 5 having 'minimal lesions', 25 being 'moderately advanced' cases, and 14 'far advanced'. All forms of collapse therapy, even when indicated, were withheld, and strict bed-rest was not exacted of any patient whose rectal temperature did not exceed 100°F. Improvement as demonstrated by radiological regression of lesions, sputum conversion or abolition, decrease in blood-sedimentation rate, and improvement in general condition, occurred in a high percentage of cases; but as in all experiments with human tuberculosis the absence of a strictly comparable control-group makes assessment of the treated group's response difficult, unless that response is outstandingly good. The most noteworthy finding was that 59 per cent of all cases treated with diasone showed sputum conversion by the end of their 4 to 5½ months' course: all 5 with minimal lesions were rendered sputum-free, as were 17 of the 25 moderately advanced and 5 of the 14 far advanced cases. This is certainly higher than the expected figure in a group of unselected patients not in receipt of collapse therapy or strict bed-rest. Moreover, in 9 of 21 cases there was radiological disappearance of cavities. It is disappointing that no mention is made of the group's body-weight before, during and after the treatment. This and similar alterations in the trend of the blood-sedimentation rate might have demonstrated whether indeed the inauguration of diasone therapy marked the turning-point in the average patient's career; for it cannot be forgotten that tuberculosis is a disease without an immediate prognosis, that remissions often occur inexplicably, and that the only certain evaluation of a therapeutic measure is the treated group's survival-value five years later, which time alone can show. Petter and Prenzlau report that the drug's toxic effects, although often well marked at first, were never unbearable or irreversible, and that most patients developed a tolerance in two or three weeks. Such is not the experience of Hinshaw, who finds diasone to be more toxic to human beings than to guinea-pigs, and the therapeutic dose for man to be unpleasantly near the toxic level. Higgins has lately shown that the toxic effects of promin on rats are much reduced when their intake of aneurine, riboflavin and pyridoxine is very large; this observation may suggest a way to reduce the toxicity of the other sulphones. The therapeutic efficacy of diasone and promizole has yet to be compared.

Weingarten's Eosinophilia

(From the *Lancet*, i, 6th May, 1944, p. 606)

EOSINOPHILIA in the tropics or in people lately returned from those regions leads to a search first for evidence of helminth infection and secondly for allergic signs. A year ago Weingarten described a chronic tropical eosinophilia in Indians characterized by respiratory symptoms, including chronic paroxysmal cough and asthma-like spasmodic dyspnoea; general symptoms, such as lassitude, loss of weight and anorexia; a curious and distinctive x-ray appearance

in the lungs, consisting of a fine, diffuse mottling not unlike miliary tuberculosis; and a well-marked leucocytosis of 20,000 to 60,000 cells per c.mm., 50 to 80 per cent being eosinophils. Organic arsenicals acted almost as a specific and were a certain cure, but without them the disease was liable to be long and exhausting, sometimes lasting for 2 to 5 years. This did not appear to be an allergic disorder, and Weingarten was unable to implicate any parasitic infection, though the response to arsenicals is suggestive of a parasitic aetiology. It was quite distinct from the transitory pulmonary infiltrations with eosinophilia described by Löffler, but seemed to be identical with the 'pseudo-tuberculous condition' reported by Frimodt-Møller and Barton. The assembly of symptoms and signs was so odd that there was some natural scepticism about the syndrome, but further cases have since been reported by others and their descriptions confirm Weingarten at every point. Simeons described 35 Indian cases seen over nine years; Chaudhuri had a typical case which responded well to mapharside (0.4 g.) injections. Emerson has reported a case in a non-Indian eight months after his return to the U.S.A. from a 4½ years' stay in India. This man was first treated for a liver abscess, apparently of streptococcal origin; six weeks after successful treatment of the abscess, weakness, fatigue and asthmatic attacks that had been present before became more prominent and laboratory investigation revealed the typical x-ray changes and the eosinophilia of Weingarten's syndrome; the patient responded well to two 10-day courses of carbarsone, 0.5 g. daily. Lately Parsons-Smith has described this syndrome in an English airman who had not been to India at all, but had been 10 months in Egypt; this man was successfully treated with neoarsphenamine injections. Thus there is now sufficient confirmation for Weingarten's syndrome to be put on the list of differential diagnosis of tropical eosinophilia, especially since it is readily treated with organic arsenicals. Its aetiology, however, remains as obscure as ever; no definite parasite has been found. A point to note is that arsenical treatment at first may temporarily increase the eosinophilia. Almost any arsenical treatment seems suitable; Weingarten used neoarsphenamine, giving a course of six injections with three days between them—0.15 g., 0.3 g. and then 0.45 g. for successive doses—the drug being dissolved in 10 per cent calcium gluconate with 200 mg. of ascorbic acid added; 'acetylarsan' and mapharside have also been used. For oral treatment acetarsol, gr. 2 twice daily for two 10-day courses, or carbarsone as in Emerson's case, have been successful. It is clear that every one in this country dealing with patients from overseas should bear the syndrome in mind.

Primary Tuberculosis Infection in Nurses

By M. DANIELS

(Abstracted from the *Lancet*, ii, 12th August, 1944, p. 201)

(a) THIS interim report analyses data collected from one of the groups under observation in the Prophit Tuberculosis Survey which was inaugurated in 1934. The methods of the survey are described.

The total number of nursing entrants to the survey up to March 1943 was 3,764. All were student nurses, drawn from two main groups of large general hospitals.

(b) Nurses were Mantoux-tested and radiographed shortly after entry to the preliminary training school. Of the 3,764 entrants, 50.3 per cent were positive to OT 1/10,000 or 1/100,000; 30.5 per cent were positive only to 1/100 or 1/1,000; 19.2 per cent were negative.

(c) The rate of Mantoux conversion in successive years of nursing training has been determined. The rate in the first year was 58.4 per cent and 78.3 per cent in the two hospital groups. The group with a higher conversion rate had a high proportion of strongly positive reactions revealing conversion. Most had no notable symptoms between the last negative test and the first positive.

(d) A study has been made of the tuberculous morbidity in nurses who entered the survey before 1942 and whose chest x-ray on entry was clear: 33 cases occurred in 452 nurses initially Mantoux-negative, 43 cases in 2,120 nurses initially Mantoux-positive. Standards of diagnosis in determining 'cases' are those laid down by the Prophit Committee.

The 33 cases arising in nurses Mantoux-negative on entry are briefly described. Analysis reveals the diversity of aspects of tuberculosis following primary infection in adults. In many cases it is difficult to determine whether the primary focus or a secondary infection is responsible for the lesion observed.

(e) The annual case-rate per 1,000 was 7.4 in nurses Mantoux-positive on entry, 18.8 in those Mantoux-negative. The rate was particularly high in the first year after Mantoux conversion.

The reasons for the lower incidence in nurses Mantoux-positive on entry are discussed.

(f) The evidence of this survey, and the combined evidence of 20 other surveys, show that the risk of development of tuberculosis following primary infection in young adults is a serious one.

It is suggested that a controlled method of anti-tuberculosis vaccination is needed. In the absence of vaccination, recommendations are made with the object of reducing the primary infection rate, detecting primary infection when it occurs, and reducing the tuberculous morbidity.

Toxicity of Sulphaguanidine

(From the *Lancet*, i, 18th March, 1944, p. 378)

SULPHAGUANIDINE has been widely used in the treatment of infective intestinal disease, and has reputation of being only very slightly absorbed and practically non-toxic. In actual fact it is much more freely absorbed and more toxic than is generally realized. It was first described in 1938 by Buttle and others, who regarded it as 'equal to sulphanilamide in activity and toxicity', and the studies of Marshall and his co-workers in 1940, from which time its popularity dates, showed that the toxicity by mouth is certainly no more and probably less than that of sulphapyridine or sulphathiazole. It was reported by them as much less readily absorbed than other sulphonamides; one dose of 6 g. per kg. body-weight gave a lower blood concentration of the drug than 0.5 g. per kg. of sulphapyridine. But crystals of sulphaguanidine derivatives are found surprisingly often in the urine, in spite of the much greater solubility of its acetyl derivative than that of sulphapyridine or sulphathiazole, showing that a considerable proportion is absorbed. Cases with toxic symptoms are already on record—thus Cole mentions a patient with ulcerative colitis who developed a morbilliform rash and vomiting due to the drug. In this issue Crofton and Diggle describe three cases of confusional psychosis arising from sulphaguanidine treatment of dysentery; their third case also developed cyanosis. The dosage in the last case was the enormous one of 10 g. four-hourly, and symptoms developed after 60 g. had been given; in the other two cases the doses were smaller, though the total was still large 87.5 g. in four days and 89 g. in five days. In another paper, Stainer and Stapleton compare the absorption and excretion of sulphaguanidine, sulphathiazole and succinylsulphathiazole (sulphasuxidine) in children, maintaining a uniform dosage of 0.05 g. per kg. four-hourly (a figure very close to that of the first two patients of Crofton and Diggle) for forty-eight hours. The total urinary excretions of sulphaguanidine and sulphathiazole in the first forty-eight hours were nearly equal, the mean values for six experiments being 27 per cent of dose given for sulphaguanidine and 25.8 per cent for sulphathiazole, but the blood levels of sulphaguanidine were only half those of sulphathiazole at a comparable time (2.14 mg. total and 1.56 mg. free drug per 100 c.c.m. compared with 4.7 mg. total and 3.45 mg. free). Smith has recently described a series of adult dysentery patients treated with sulphaguanidine, many of whom developed toxic rashes

about the ninth day; the blood sulphaguanidine level, on doses of 24 g. daily, was 10–14 mg. per 100 c.c.m. Jamieson, Brodie and Stiven have also shown that considerable amounts of sulphaguanidine are found in the urine of patients receiving therapeutic doses of the drug, and Whyte has observed sulphonamide crystals in the urine of 18 out of 25 patients given a week's course of sulphaguanidine totalling 51 g., 14 of them having red cells as well in spite of a fluid intake of over 5 pints a day. Sulphasuxidine stands on a different plane; under the same conditions less than 2 per cent of the drug ingested is found in the urine, and traces only in the blood. In surgical practice, with the large initial 'loading dose' usually given, measurable quantities are sometimes found in the blood, although the level is always very much lower than that of the other compounds.

It is not yet possible to decide on the relative value of the various sulphonamides in the treatment of intestinal infections, and Paulley has suggested that sulphapyridine has advantages over the more widely used sulphaguanidine. It is clear however that sulphaguanidine is a readily absorbed drug, and one capable of giving rise to toxic symptoms, and that adequate urinary output must be maintained to prevent the drug crystallizing out. This is of particular importance since the conditions for which the drug is usually given—dysentery and dysentery-like illnesses—tend to a small output of concentrated urine unless energetic measures are taken. Sulphaguanidine is to be treated, like all other sulphonamides, as a valuable but potentially dangerous drug, and should not be exhibited in reckless dosage, as is the habit in some quarters to-day. Sulphasuxidine and possibly other drugs of the same type, in which an acyl-substituent group is attached to the NH_2 group of sulphathiazole, seem to be free from this danger, and to live up to their reputation of being very poorly absorbed.

Reform of Medical Education

(From the *British Medical Journal*, ii, 22nd July, 1944, p. 117)

Few bodies in the history of British medicine can have had a greater opportunity or more responsibility than the Interdepartmental Committee appointed in March 1942, under the chairmanship of Sir William Goodenough 'to inquire into the organization of medical schools, particularly in regard to facilities for teaching and research and to make recommendations'. Progress in the science and art of medicine is inseparably connected with the facilities which our medical schools provide to attract the right men and to enable them to do their best work. The doctor's service to the community depends not only on his innate gifts but on the way in which he has been trained to think and do. And so the nature of medical education and the organization and facilities of our medical schools are some of the most potent factors in shaping the standard of medicine. At no previous time has there been an opportunity to survey the whole of medical education, in order to remedy its defects, with more certainty that something must be done. Change is inevitable; the destruction wrought by war and the people's desire for an improved health service make it so.

This eagerly awaited and now published report is a long one—312 pages, including 28 pages of summary—and it is impossible here to note more than a few of its chief points. The way is to be made easier for the student. All medical schools are to become co-educational. To increase the field from which students are selected, increased financial grants and a simplified machinery for distributing them are recommended. Students should not be selected on examination results alone. Accommodation should be provided in halls of residence for part of the undergraduate period, and for specific purposes in hospital during part of clinical training. The instrument of medical education should be a medical teaching centre catering for a student entry of 80 to 100 for the clinical years; and it should

comprise a medical school which should be a faculty, college, or school of the university, a parent teaching hospital of 950 to 1,000 beds, and a group of neighbouring hospitals and clinics to provide supplementary facilities for clinical teaching. The governing bodies of medical school, parent teaching hospital, and associated teaching hospitals are to remain separate, but their work is to be co-ordinated by interchange of personnel and through common advisory machinery for selection of staff. In the main the details as to how these objects should be attained are left to the schools themselves. Important suggestions relating to certain schools are, however, made. In Scotland the three extramural schools in Glasgow and Edinburgh, which, receiving no Government grants, compare unfavourably with the university schools, are to disappear. In London the facilities provided by the West London Hospital should lapse after some years; to harmonize with the redistribution of population, Charing Cross is advised to move to a site in Middlesex, St. George's to South London, and the London School of Medicine for Women to North London. All are to be complete schools in that preclinical as well as clinical facilities are to be provided, and all are advised to conform to the ideal size and pattern already mentioned. The proposal to provide in Oxford complete clinical facilities for a small number of undergraduates is approved, and the very important recommendation is added that this school should experiment in teaching. Cambridge is unsuitable at present for undergraduate clinical teaching; it should first develop postgraduate departments. No new medical schools are to be created. In view of the importance of the universities and medical schools to any national health service, they should be represented on such central and local councils as may be set up for administration.

The report points out that the accommodation and equipment of most medical schools and teaching hospitals fall far short of what is necessary for teaching and research, and recommends that grants be made to remedy these deficiencies. Teachers in both preclinical and clinical departments should be more numerous and better paid. A national range of salaries with upper and lower limits is suggested: for example, at pre-war values professors would receive between £1,500 and £2,500, demonstrators between £350 and £500, and whole-time physicians or surgeons between £1,000 and £2,000 a year, part-time teachers being remunerated proportionally to the time they give. The teaching staff in all preclinical departments and in pathology should be whole-time. As suitable men become available, every school should aim at securing whole-time professors of general medicine, surgery, and obstetrics and gynaecology; in the special departments it may sometimes be desirable for men to work whole-time in the teaching centre. Most senior clinical posts would remain part-time, but the junior posts would be full-time. All appointments should be made from the widest possible field of applicants, and above that of registrar by a small advisory council including outside experts and representing the hospitals concerned, the university, or school.

Recommendations concerning the curriculum resemble in broad outline, though differing in certain important details from, those made by the College of Physicians. Elementary physics, chemistry, and biology should be taught at school as part of general education, and continued at the medical school as part of the course in anatomy and physiology. The standard required for entry to a medical school should be midway between that of the principal and subsidiary subjects of the Higher Certificate. Preclinical subjects should be pruned of some detail and more closely co-ordinated with each other and with clinical studies. In the clinical period the main emphasis should be on basic principles and methods, and on the future requirements of the general practitioners. The important recommendations are made that much of the teaching of operative surgery and gynaecology should be reserved for the postgraduate training, of specialists. In the undergraduate period the chief emphasis in surgery should

be on principles, and on the recognition, early treatment, and ultimate effects of conditions commonly met in general practice. The Committee recognizes the difficulties raised by the growth of specialism in the teaching of general medicine and surgery, and recommends, that to facilitate co-ordination the teaching centre should be organized into divisions of (1) pre-clinical studies, (2) pathology, (3) medicine, (4) surgery, and (5) obstetrics and gynaecology, each with academic heads. Senior teachers whether whole-time or part-time, would have now the unfettered control of the management of their patients. The importance of social medicine, psychiatry, and child health is stressed and the desirability of students' residence during part of their training pointed out. The undergraduate course should last four and a half years, of which the first two should be preclinical. It should terminate in a final examination conducted by the university and be succeeded by a compulsory year of house appointments, on satisfactory completion of which the student would be admitted to the *Medical Register*. The qualifying examinations conducted by licensing bodies other than the universities should cease. It is pointed out that these cater chiefly for the extramural students in Scotland and for the students of the London Medical Schools. It is considered that if the Universities of Oxford, Cambridge, and London make their examinations conform more to the type of internal examination held elsewhere, then there should be no need for these extra examinations, which may interfere with the teaching programme of the school and which cost the student money. The Committee feels that the overhaul of the whole undergraduate curriculum and a reduction in its content are so important that their accomplishment might be made a condition of any increase in the Exchequer grant for undergraduate medical education. The initiative in this matter is referred to the General Medical Council.

No reform in undergraduate medical education can be effected without the provision of proper machinery and facilities for postgraduate study. Recommendations in this respect may be considered under two heads, those for the training of teachers and specialists and those for general practitioners. For specialists and consultants the Committee accepts the recommendations of the Royal Colleges that five years' training after registration is necessary. These five years are to be spent in paid appointments in general hospitals, scientific laboratories, special hospitals, and abroad. Diplomas in public health, clinical pathology, bacteriology, and tropical medicine should be awarded by the universities, the remainder by the Royal Colleges. It is considered that the only ultimately satisfactory postgraduate training for the general practitioner is his continuous contact with the work of hospitals and specialists through holding suitable clinical assistantships. But for many years refresher courses will be necessary, and these should be organized by the universities having medical faculties, and held, if possible, at institutions not undertaking undergraduate education. These recommendations imply the development of special hospitals as centres of postgraduate education and research, and far-reaching proposals are made for the development of the British Postgraduate Medical School in London as a federation of general and special postgraduate institutes. The implementation of these proposals will naturally cost money. The Committee estimates that to meet recurrent expenditure on undergraduate and postgraduate medical education the university schools will need additional resources which within 10 years will amount to between £1,750,000 and £2,500,000 a year, depending on expansion to meet a need for more doctors. Capital expenditure on the university medical schools is estimated at pre-war costs to be not less than £5,000,000. Finally, an Exchequer grant of £500,000 to the teaching hospitals is recommended provisionally as payment for the extra costs incidental to the provision of facilities for teaching and research. All these grants should be made through the Universities Grants Committee.

The present arrangements for medical education may be likened to a neglected garden, and these proposals to the plants of the gardener to remove weeds and dead wood and encourage growth where it promises to be productive. If the plans are carried out we may anticipate that the garden will be tidy, decorative, and above all productive. Two chief obstacles lie in the way. The first is the expense, in view of the uncertain economic condition of the country in the post-war period. But considering the relatively small sums involved, and the advantages that would be reaped by its children and its children's children, it would be short-sighted of the nation to allow difficulties of this kind to stand in the way. The second obstacle is the men. Teachers of medical students are to be given the tools so that they can finish the job. But unfortunately the post-war years will see a greater dearth of trained teachers than there has been since the end of the last war. Since 1939, staffs, particularly in the clinical departments, have been cut to the bone, and the best young men have been absorbed in the Services. If, then, the opportunity is to be taken, it is essential that our medical schools should begin as soon as possible to make more junior teaching and research appointments. The men must be trained now so that they can use the tools.

Administration of Pentothal

By F. W. ROBERTS

(Abstracted from the *British Medical Journal*, i, 17th June, 1944, p. 825)

TECHNIQUE OF INJECTION

1. NEVER use a stronger solution of pentothal than 5 per cent—i.e. $\frac{1}{2}$ g. in 10 c.cm.
2. Use a 10-c.cm.-capacity eccentric nozzle syringe. This size is handier to hold than a 20-c.cm. and by its size will limit any injection to $\frac{1}{2}$ g. The eccentric nozzle makes venepuncture easier.
3. Use sharp, short-bevel needles.
4. Have your patient in a stable position, so that when he relaxes, he will not slump into a new position.
5. Be stable and comfortable yourself; sit, stand, or kneel at your convenience; do not balance on one leg and support the patient's arm on the other knee, and do not bend down over a very low bed.
6. Test the intravenous position of your needle point by aspirating blood back before you inject.
7. Inject slowly, watching: (a) the patient for developing unconsciousness and continued respiration; (b) the needle point to be sure you are still in the vein; (c) the syringe to see how much you are giving.
8. Lastly, but most important, keep the airway clear.

DOSAGE

There is no fixed dose. The amount that each patient needs can be determined only at operation by his reaction to the drug as it is administered. While the first few c.cm. are administered slowly the patient should be watched, his reactions to simple questions noted until he is seen to be asleep. He has now had the *sleep dose*. He will need for induction or any very short anaesthesia a total of at least twice the sleep dose. The initial injection should never exceed a total of three times the sleep dose. More pentothal may be necessary during the operation; each such subsequent injection should not exceed the sleep dose.

SHOCK

Extra care should be taken in shocked patients to determine the correct dose, which is always much smaller than in normal patients. Halford (*Anaesthesia*, Jan. 1943) reports several fatal injections of 0.5 g. in shocked Pearl Harbour casualties, and I am not surprised. This shows that Dr. Montuschi's injunction is not enough. On the other hand, in the same volume of *Anaesthesia*, Adams and Gray report successful extensive thoraco-abdominal surgery in a shocked woman, using repeated very small doses.

Reviews

NON-PULMONARY TUBERCULOSIS.—By Michael C. Wilkinson, M.B., B.S., M.R.C.S., L.R.C.P. 1942. Hamish Hamilton Medical Books, London. Pp. xvi plus 174. Illustrated

THE term non-pulmonary tuberculosis usually refers to that form of the disease which affects bones, joints, glands and abdominal organs such as kidneys, caecum, fallopian tubes, etc. Such tuberculosis is much less common in India than in western countries, but it is not so rare as is often believed; for instance, tuberculous adenitis of the neck is said to be fairly common especially among certain hill tribes. In any case, all these forms are at times seen in practice. When a practitioner requires some guide, we feel sure that the little book before us will serve the purpose well. It is chiefly devoted to description of treatment, and indications for both conservative and surgical methods are given. The chief value of the book lies in the fact that it is based on the author's own experience derived from investigations and treatment of a series of five hundred and ninety-three patients admitted to a sanatorium during the period 1930-37.

R. N. C.

DISEASES OF THE CHEST.—By Robert Coope, M.D., B.Sc., F.R.C.P. 1944. E. and S. Livingstone, Edinburgh. Pp. xii plus 524. Illustrated. Price, 25s.; postage, 9d. (home)

'NOWADAYS chest physicians are perhaps more devoted to the x-ray viewing box' comments Dr. Robert Coope, 'than to the post mortem table, for in recent years radiology has brought exciting advances in diagnostic methods'; but 'radiological interpretation needs to be controlled by knowledge of the normal, and subjected to the confirmation and correction of pathology'. At present there are, he continues, an undue scepticism about the physical signs, a disproportionate reliance on radiograms, and too easy an acceptance of purely radiological diagnoses which have as yet no clearly proved pathological picture. With these ideas in the background, he has written this book, and we believe he has been successful. Its arrangement is on somewhat unorthodox lines. After describing the diagnostic methods, the author starts with the diseases with collapse of the lung and then some bronchial conditions, and these are followed by common cold and influenza. Oxygen therapy comes next and then follow other diseases of the chest, including a long chapter on chest injuries. This arrangement in no way affects the value of the book which impresses one with its clinical character. It is pleasant to read; there is no overburdening with long lists of signs and symptoms, and the advice given under treatment is sound and practical. We notice that one or two paragraphs have been given to a description of Loeffler's syndrome, but there is no mention of 'eosinophil lung' or 'tropical eosinophilia', a subject which is assuming some importance in the tropics and which possibly may be carried to temperate countries through servicemen from overseas. The book is illustrated with many good diagrams and thirty-four x-ray plates, among which might be included one or two showing atypical pneumonia, a disease which, whatever its pathological nature, has caused epidemics in recent years and which can definitely be diagnosed only by x-rays.

R. N. C.

A GUIDE FOR THE TUBERCULOUS PATIENT.—By G. S. Erwin, M.D. 1944. William Heinemann Medical Books Ltd. Pp. viii plus 115. Price, 3s. 6d.

'In no other disease of common occurrence is the intelligent co-operation of the patient more necessary, both during and after the period of hospital or sanatorium treatment, for the outcome of such treatment

can be influenced materially, for good or evil, by the patient himself.' These words from the preface indicate the object of writing this book, *viz*, to provide him with some knowledge of the disease from which he suffers, to make that co-operation easier. In as non-technical language as possible, the author relates the causes of pulmonary tuberculosis, symptoms, methods of examination and treatment at home and institutions and thereafter. There is a chapter on non-pulmonary tuberculosis as well. The advice given to patients in the booklet is wise and practical. We have however one or two comments to make. Under the 'causes of tuberculosis' it is said that the disease is caused by tubercle bacillus, but there is no mention that the effect is produced by infection of the lung, although the author was obviously talking about the pulmonary condition. A diagram of the respiratory organs might also add to the interest in the subject. In reading this book a tuberculous patient will naturally try to find out the prospect of his own recovery, and although explanation to a layman may be a difficult matter, more might have been profitably said about prognosis than is given on page 56.

R. N. C.

CLINICAL PRACTICE IN INFECTIOUS DISEASES.—

By E. H. R. Harries, M.D. (Lond.), M.R.C.P., D.P.H., and M. Miltman, M.D. (Lond.), M.R.C.P., D.P.H., D.M.R.E. Second Edition. 1944. E. and S. Livingstone Ltd., Edinburgh. Pp. viii plus 570. Price, 22s. 6d.

MANY years ago the reviewer was first the student and later the house physician under the first named author and he remembers the excellent teaching given. This book which is now in its second edition brings that teaching up to date. The book includes general chapters on notification, infection resistance, hypersensitiveness, allergy, serum reactions, transmission, diagnosis, epidemiology and control, management of infectious diseases including isolation, drugs and diet, and control of infectious diseases in hospital. Twenty-five chapters deal with the different infectious diseases one by one. An invaluable book to the student and the practitioner.

A SYNOPSIS OF HYGIENE (JAMESON AND PARKINSON).—

By G. S. Parkinson, D.S.O., M.R.C.S., L.R.C.P., D.P.H., Lieut.-Col., R.A.M.C. (Retd.), and G. P. Crowdon, O.B.E. Eighth Edition. 1944. J. and A. Churchill Ltd., London. Pp. xvi plus 719. Price, 25s.

THIS well-known book is now in its eighth edition. Parts of the old appendices have been omitted. Recent work on chemotherapy, venereal diseases, typhus fever, yellow fever, infective hepatitis, and leptospirosis has been discussed. A summary of the government proposals for a national health service is included. This book gives a mass of information on all aspects of hygiene.

A TEXTBOOK OF HISTOLOGY FOR MEDICAL STUDENTS.—

By Evelyn E. Hewer, D.Sc. (Lond.). Third Edition. 1944. William Heinemann Medical Books Ltd., London. Pp. viii plus 384. Price, 17s. 6d.

THIS excellent textbook of histology for students is in its third edition. Some revision has been made since the last edition. This book has been widely acknowledged as a most excellent textbook for medical students.

AN ATLAS OF THE COMMONER SKIN DISEASES.—

By Henry C. G. Semon, M.A., D.M. (Oxon.), F.R.C.P. (Lond.). Second Edition (reprinted 1943). John Wright and Sons Ltd., Bristol. Pp. viii plus 272

THIS is a reprint of the second edition which was published in 1940. The main attraction of this book is its excellent reproductions numbering 120 of colour photography of the living subject.

Abstracts from Reports

FIFTH ANNUAL REPORT OF THE TUBERCULOSIS ASSOCIATION OF INDIA, NEW DELHI, FOR THE YEAR 1943

In spite of war-time difficulties the Association carried on its usual activities during the year.

In the *Lady Lintithgow Sanatorium* two military wards of 40 beds and 14 new cottages were completed, thus the number of beds increased from 136 to 190, of which 30 are in private wards. The Association has endowed one bed at a cost of Rs. 20,000 in commemoration of Lady Lintithgow as Foundress of the Sanatorium. A fund for poor patients has been opened with an initial donation of Rs. 1,000 from Lady Lintithgow and bears her name. This will be utilized on providing forms of treatment, comforts and allowances for poor patients. There were 98 patients at the end of 1942, and 216 new admissions were made in 1943. The number of patients discharged during the year was 147, leaving 167 on the roll at the end of 1943.

The *New Delhi Tuberculosis Clinic* has maintained its position as a model treatment and teaching centre. A total of 3,309 patients were treated during the year.

Doctors P. V. Benjamin and T. J. Joseph acted as honorary technical advisers. The publicity and propaganda work has been continued as usual. A new publication, 'Directory of Tuberculosis Institutions in British India and Indian States' has been brought out. Dr. Benjamin broadcast a talk on 'the war against tuberculosis'. Other features included the issue of a special tuberculosis number of the *Indian Medical Gazette*, and a competition for the award of the Hassan Masud Suhrawardy Memorial Anti-tuberculosis Challenge Shield which was won by the Bombay Municipality.

A post-graduate course in tuberculosis was held under the auspices of the Central Association at Hyderabad-Deccan at which 17 candidates received training. Moreover, three doctors completed intensive training for 6 to 9 months at the above mentioned sanatorium and the clinic. One health visitor was also trained at the clinic.

One more association—the Mysore State Tuberculosis Association—was affiliated during the year; so there are now 14 provincial and 16 State associations affiliated to the central organization. Six clinics, one sanatorium and one hospital were also opened during 1943; eight clinics are under construction and proposals for construction of ten more are under consideration.

All the affiliated associations have maintained a well-organized anti-tuberculosis campaign.

ANNUAL REPORT OF THE UNION MISSION TUBERCULOSIS SANATORIUM, AROGYA-VARAM, NEAR MADANAPALLE, SOUTH INDIA, FOR THE YEAR 1942-43

THE training of doctors for Tuberculosis Diseases Diploma of the Government of Madras has continued as usual. A class of nine women completed the laboratory training, and from July the first course of training for a laboratory diploma began with eight students, three women and five men. Several extensions and improvements to buildings are under consideration.

There are sixteen ex-patients in the colony. The business of the colony stores has grown considerably, and its sales increased from Rs. 75,903 in 1941-42 to Rs. 1,14,173 during the year under review. Printing, weaving and tailoring are carried out. A rope-making machine will soon be put into use.

The number of patients remaining from the previous year was 255, and during the year 457 patients were

admitted and 460 discharged. The number of beds has increased to 254 from 109 in 1915. There are 9 general and 107 special wards.

Dr. P. V. Benjamin, Medical Superintendent, has been appointed honorary adviser to the Tuberculosis Association of India.

The report records with deep regret the death of Dr. C. Fridodt-Möller on 24th March, 1943, after an illness of nearly a year and half. His death is not only a loss to the sanatorium but to tuberculosis work all over India as well. Under his leadership the sanatorium came to be recognized as a premier tuberculosis institution in India. It has been decided to form a foundation in his memory in order to promote research in tuberculosis, for which a sum of at least Rs. 1,00,000 will be required.

Correspondence

THE MEDICAL PROFESSION IN INDIA AND ITS EDUCATION

Sir,—In view of Colonel McRobert's article on Indian Degrees for Indian Graduates, the experiences of two candidates for the recent M.R.C.P. examination held at Poona may be of interest. Both failed, though one survived to the semi-final round and the other to the final round. Both had failed more than once at the M.D. examination of their respective Indian universities. Both assured me that they would appear again for the M.R.C.P. with hope and confidence, but dreaded another appearance at their M.D. The reason given was, that all the M.R.C.P. examiners appeared to wish them to pass, while some of the M.D. examiners appeared to wish them to fail. In other words some of the M.D. examiners were hostile.

If, as Colonel McRobert points out, medical examinations, even for the higher degrees, should be conducted solely for the purpose of ascertaining if the candidate has reached the required standard in the subject in which he is being examined, then there is no place for the hostile examiner.

The hostile examiner is even more of a menace in the examinations for the ordinary pass degree or diplomas. I would count as hostiles, those puffed up with self-importance who will not abide by the rules for their guidance, and for example by passing only a percentage, convert a pass examination into a competition. Those lack the qualities necessary for a good examiner, tact, courtesy, and patience with the candidate, and a sympathetic knowledge of student mentality. These latter have been cast in the wrong part. The remedy lies with the examining bodies, who by an adequate system of inspection should ensure their examiners are competent and are conducting their examinations according to the rules laid down.

As far as the licentiate class is concerned, with whom alone my experience lies, that such inspections are so seldom carried out is mainly because of the expense involved.

Licentiate education is the responsibility of the eleven Provinces, while graduate education is that of the Centre acting through the Medical Council for India.

The Provinces have a great many other interests, far more important to them, than that side of medical education which has been thrust upon them. They are always disinclined to open their purse strings.

It should be realized that a subject so vital as medical education cannot but be treated as a whole for the whole of India, including the Indian States. It is continually forgotten that the States comprise 1/3rd the area and 1/4th of the population of the sub-continent.

If all medical education in India were controlled by one single body such as the Medical Council for India, then that body, by withholding recognition, could insist that those responsible for medical educational

establishments, provided them with proper equipment, staff, buildings and finances, and that examining bodies and their examiners conducted their examinations on a sound basis.

Uniform central control would enable the second point raised by Colonel McRobert, that licentiates should be given facilities to obtain a degree, to be treated radically. If medical education was treated as a whole and not in bits, and the profession was one body not two, then the licentiate and his diploma would fall into their natural place as the foundation of the system on which the profession and its education were based.

It is overlooked that both the graduate and the licentiate start from the same common point, the matriculation or its equivalent. This, then in practice is the standard of general education demanded as the portal for either party to enter the medical profession.

It is true that before entering a medical college the would-be graduate has to pass the Intermediate Science Medical Group, and that admittedly the average student entering a medical college is better educated than the average student entering a medical school. But the reason is not that two years' study of science has improved his general education, but the fact the expenses involved in the two years' course at a science college, and the prospects of the expenses of the five years at a Medical College limit the intending graduates to a wealthier and therefore a generally better educated class than the average intending licentiate. Who would not rather be a graduate rather than a licentiate, if he could afford it? It is overlooked that the licentiate is considered to be a doctor all over India. In large areas he is the only doctor practising western medicine. He exists in far larger numbers than the graduate. He has been admitted into the I.A.M.C. as a doctor, where his position with regard to the graduate is not unlike that of the graduate to his colleague with a higher degree ranking as a specialist.

The standard of qualification required of the licentiate is therefore in practice the minimum standard of qualification required for a doctor in India.

Why not recognize the fact and build up the system of medical education in India, and organize the medical profession, with the licentiate as the foundation?

At the conference on medical schools held at Delhi in 1938, Sir Hari Lal Gosalia, an experienced administrator and the only layman present, pointed out that the abolition of the licentiate in favour of the far more expensive graduate, would set back the extension of the health services into the country districts, perhaps indefinitely.

With the news from France as it is, rightly attention is being given to post-war reconstruction.

The calculation has been made as to the number of doctors India now possesses, and the number she should possess in that 'bright future' which we are told is before us. The answer to that sum is a very large figure. The calculation as to what the cost of producing and maintaining the large number of doctors required for the future has not I think yet been made. When it is it will be found that the final figure is colossal.

India is a relatively poor country and the finding of colossal sums for this and that is beyond her capacity.

There is no shame in being poor, or of having to cut one's coat according to one's cloth. Britain is poorer than the U.S.A. and Scotland than England. What Scot admits inferiority to the Englishman, or Englishman to the Yank?

If the very large number of doctors that India undoubtedly needs are to be provided, the majority of them must be produced cheaply, so that the money spent on their training will be commensurate with what they may expect to earn when trained.

In any profession, when the ordinary earnings of the average man do not offer a reasonable return on the time and money spent in entering that profession, then the loss indubitably will be made up, inevitably by dubious means.

Before this war many medical graduates were forced by economic stress to accept posts usually held by licentiates, and on the pay of licentiates. Labouring under such conditions, is it to be wondered at that the ethical standards of the medical profession in India are not high? The fault lies not with the individual members of the profession, but with those who allow such conditions to arise.

Let the foundation of the medical profession in India be the licentiate, primarily providing what all systems of medical relief must rest on, the general practitioner.

The licentiate should be produced as cheaply as is consistent with the acquisition of a sound general knowledge of that aspect of his profession he will ordinarily be engaged in, i.e. that of a general practitioner in the country.

While ensuring that the school and hospital in which he is trained are not allowed by financial starvation to remain in the pitiable condition portrayed by General Sprawson in his note on Medical Schools of 1935, it should be recognized that it is not necessary for these establishments to be equipped with every latest gadget, to be housed in palaces, or be staffed entirely by holders of the F.R.C.S. and M.R.C.P.

There is a happy mean not impossible to arrive at, and maintain, provided there is one strong single body to exercise control. In devising the curriculum it should not be necessary to demand the steps of advanced operations which the student is never likely to have to perform. Endeavour should be made to concentrate on the common diseases, their recognition, treatment, and prevention, under conditions the student will probably deal with them in the future, that is to say, without the aid of a large well-equipped hospital behind him. Too much time need not be spent on midwifery. The assumption should be that the student, unless a woman, is unlikely to practise midwifery as the British G.P. used to and now does not. Since the majority of this class of practitioner will never leave India, it is unnecessary to insist on a standard that will gain recognition for registration by the General Medical Council of Great Britain.

It should be remembered that examinations can be made easy without any lowering of the standard. The London M.B.B.S. used to be more difficult to pass than the English Conjoint, because it was held only every six months, and all subjects in each of its two groups had to be passed together. The Conjoint was held quarterly, and each subject could be passed separately. Its standard however was the same required for the London M.B.B.S., possibly higher, as with a far less penalty for failure, the examiners tended to be stricter. It would certainly lessen the cost of obtaining the Licentiate Diploma if the examinations were held quarterly and if the subjects could be passed separately.

What the length of the licentiate course should be is debatable. The need for economy points to the retention of the present average of four years for the preclinical and clinical courses, but I doubt if the bare essentials required can be covered in under five years by the class of student that has to be dealt with.

A sound grounding in science is no doubt an excellent foundation for a medical career, for those who can afford the time and money to undertake more than the bare essentials. The bare requirements in science should not take two years to attain. The London University only requires nine months to be spent of the pre-professional course.

Let there be a special pre-professional course for licentiate not exceeding nine months, but including, besides the usual science subjects, a strong course in English designed to enable the student to marshal his thoughts and express them clearly and concisely. The medical colleges should lead to degrees and diplomas the equivalent of the present Schedule I and as such be recognized as registrable by the G.M.C. of Great Britain. The licentiates might form a third schedule, Schedule III.

The medical colleges should be left to those with the time and money to pass through them. Such students would be the counterpart of the British student

lucky enough to have, or to gain by scholarship; the means to proceed to Oxford or Cambridge, rather than to the degree of a more prosaic Provincial University, or to the diploma of one of the Conjoint Boards.

If unification of the medical profession in India is to be attained, it is essential that at least the best of the licentiates can proceed without too much expenditure of time and money to a Schedule I degree or diploma. This could be achieved by allowing all who pass their intermediate licentiate examination with honours to proceed to a Schedule I degree or diploma without further examination in anatomy or physiology. Those failing to obtain honours could be allowed to proceed after a further six months' period of study for, and the passing of, a special examination of the standard of a 2nd M.B.B.S.

To proceed to the finals of a Schedule I degree or diploma, consideration should be given to licentiates passing their own final with honours, or who have put in a recognized time, at a recognized institution, in a recognized post as H.S. or H.P.

Such a system would probably necessitate the affiliation of licentiate granting bodies with universities, or other bodies granting Schedule I diplomas. A central authoritative guiding body would go far to help bring about such measures.

No system of medical education could be complete without those diplomas for the special subjects, the necessity for which, and whose proper use are so ably explained by Colonel McRobert.

Again to ensure that those who are responsible do not pervert their use and allow all members of the profession to have reasonable access to them would be difficult without that central body controlling all medical education in India which it is the object of this letter to advocate.

M. A. NICHOLSON,
LIEUTENANT-COLONEL, I.M.S.,
Chief Medical Officer, Central
India and Superintendent, King
Edward Medical School, Indore

INDORE,
19th September, 1944.

UNIVERSITY OF MADRAS

SIR,—The University of Madras is organizing through the Council of Post-Graduate Medical Education the first course of post-graduate lectures commencing on the 5th January and extending over a period of three months. The course comprises lectures in Medicine, Surgery and Obstetrics and Gynaecology, and not less than 20 lectures will be arranged under each of these branches. Particularly the lectures arranged in February will serve as a Refresher course for the general practitioner. A notice about this is given below:—

'The Post-Graduate Courses in Medicine organized by the Council of Post-Graduate Medical Education in this University will be inaugurated by His Excellency the Governor and Chancellor of the University on Wednesday, the 3rd January, 1945, at the Banqueting Hall, Government House, Madras.'

'Post-Graduate Courses of Lectures in Medicine, Surgery and Midwifery will be held from the 5th January onwards till the end of March in the City Hospitals, and will consist of over 20 lectures in each of these subjects. The course of lectures in February is specially intended as a Refresher course for the general practitioners. All members of the medical profession who are desirous of taking the course can attend the complete course of lectures or any part thereof on payment of the fee of Rs. 100. Further particulars can be had from the Honorary Secretary, Council of Post-Graduate Medical Education, University Buildings, Chepauk, Madras.'

C. R. GANAPATI,
Acting Registrar.

UNIVERSITY BUILDINGS,
CHEPAUK, MADRAS,
1st December, 1944.

Service Notes

APPOINTMENTS AND TRANSFERS

IN exercise of the power conferred by clause (a) of sub-section (1) of section 3 of the Indian Medical Council Act, 1933 (XXVII of 1933), the Central Government is pleased to nominate Colonel Norman Briggs, M.R.C.S., D.P.H. (Eng.), I.M.S., Inspector-General of Civil Hospitals, United Provinces, to be a member of the Medical Council of India from the United Provinces, with effect from the 7th November, 1944, *vice* Major-General D. P. Goil, I.M.S. (Retd.).

The undermentioned Colonels of the Indian Medical Service have been appointed Honorary Physicians to The King, dated 29th October, 1943 :—

Colonel A. C. Macraw, V.H.S., *vice* Colonel C. A. Wood, M.C., retired.

Colonel R. V. Martin, C.I.E., V.H.S., *vice* Colonel R. Sweet, D.S.O., retired.

Colonel J. B. Hance, C.I.E., O.B.E., V.H.S., appointed Honorary Surgeon to The King, with effect from the 9th August, 1943, *vice* Colonel T. C. Boyd, Indian Medical Service, retired.

Lieutenant-Colonel H. J. Curran, Civil Surgeon, Dacca, on relief, is appointed as Inspector of Hospitals, Dacca.

His Excellency the Governor of Bengal has been pleased to make the following appointments on his personal staff, with effect from the 23rd August, 1944 :—

Major J. Brebner, M.B.E., Civil Surgeon, Darjeeling, to be Honorary Surgeon to His Excellency in Darjeeling, *vice* Lieutenant-Colonel G. H. Mahony, I.M.S. (Retd.).

Major W. J. Virgin, on arrival in Bengal, is appointed as Civil Surgeon, Dacca, with effect from 24th October, 1944, *vice* Lieutenant-Colonel H. J. Curran.

Major L. S. F. Woodhead is appointed to hold medical charge of the Civil Station of Barrackpore, with effect from the 11th October, 1944, *vice* Major F. E. Adams, R.A.M.C.

Major G. B. W. Fisher, Surgeon Superintendent, Presidency General Hospital, Calcutta, is appointed temporarily to be an Honorary Surgeon to His Excellency in Calcutta, *vice* Lieutenant-Colonel F. J. Anderson, C.I.E., I.M.S. (Retd.).

The undermentioned officers are transferred to the General Service Cadre with effect from the date specified :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE SECONDED TO INDIAN ARMY MEDICAL CORPS (Emergency Commissions)

Captain Sessa Padmanabhan Iyer. Dated 19th September, 1944.

To be Captains

Ramesh Chandra Sharma. Dated 12th December, 1943.

Gordhandas Vallabhdas Parikh. Dated 20th July, 1944.

Sachindranath Das Gupta. Dated 14th August, 1944.

Ikara Zacharias Thomas. Dated 20th August, 1944.

Kalipada Datta. Dated 20th August, 1944.

Simao Garlos Dos Remedios. Dated 9th September, 1944.

Belle Sanjiva Rao. Dated 20th September, 1944.

Sadhuram Pahlajrai Notani. Dated 21st September, 1944.

To be Lieutenants

Hassan Ramaswamiyengar Varadarajan. Dated 9th August, 1944.

Shah Shamsuz Zoha. Dated 11th August, 1944.

Krishan Kumar. Dated 14th September, 1944.

Pushpala Venkat Rao. Dated 21st September, 1944.

14th August, 1944

Tanjore Krishnaswamy Jayaram.

Anantha Krishnan Nilakantan.

Codati Visakam.

Vengarai Krishnaswamy Visvanathan.

15th August, 1944

Samuel Gopalswamy Ramaiya.

18th August, 1944

Subramaniam Venkataraman.
Natesan Narayanasamy.

19th August, 1944

Viswanatha Ramachandran.

Puvadan Thayyan Balrama Varma.

Ganapathi Agraharam Subramania Krishnamurti.

Manakkal Ganesa Varadarajan. Dated 20th August, 1944.

21st August, 1944

Mahadev Anant Gokhale.

Muhammad Ubeidullah.

Gnanaprakasam Venkatappan.

6th September, 1944

Gur Bux Singh.

Abdul Majeed Jafar.

Ata-ul-Haq Chaudhuri. Dated 10th September, 1944.

20th September, 1944

Harbans Singh Anand. Hame Durgu Singh.

The undermentioned officer retires with gratuity and is granted emergency commission from the date specified :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Short Service Commission)

Captain Mohammad Seraj-ul-Haque. Dated 24th June, 1944.

The undermentioned officer is seconded to the Indian Army Medical Corps :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE (Emergency Commission)

Captain L. D. Kale. Dated 10th June, 1944.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commission)

To be Lieutenant

Narain Bulchand Thadani. Dated 3rd June, 1944.

The undermentioned officer of the I.M.S. (E.C.) reverts from I.A.M.C. and is seconded for service with the Royal Indian Naval Volunteer Reserve :—

Captain S. K. Chopra. Dated 13th October, 1944.

The undermentioned officers are seconded for service with the Royal Indian Navy, with effect from the dates shown against them :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE (Emergency Commission)

Captain G. E. J. Burby. Dated 5th August, 1941.

Captain (A/Maj.) G. N. Rodgers. Dated 23rd April, 1942.

The undermentioned officer of the I.M.S. (E.C.) reverts from I.A.M.C. and is seconded for service with the Royal Indian Navy :—

Lieutenant E. A. Sinclair. Dated 10th October, 1944.

The undermentioned officers of the I.M.S. (E.C.), have been granted Emergency Commissions :—

INDIAN AIR FORCE—MEDICAL BRANCH

To be War Substantive Flying Officer

Lieutenant Nawab Khan. Dated 8th July, 1944.

To be War Substantive Flight-Lieutenants

Captain Meenakshi Sundaram Muthukumarasami. Dated 3rd July, 1944.

Captain Jas Raj Kumar. Dated 19th July, 1944.

Captain Amalendu Das Gupta. Dated 11th August, 1944.

(WOMEN'S BRANCH)

To be Captains

Miss Beatrice Mary D'Souza. Dated 1st August, 1944.

Miss Puthuzeril Puthenpurakal Elizabeth Kuriyan. Dated 5th September, 1944.

INDIAN MEDICAL SERVICE (FOR SERVICE WITH THE ROYAL
INDIAN NAVY)

(Emergency Commission)

(WOMEN'S BRANCH)

To be Captain

Miss Daisy Pereira. Dated 4th September, 1944.

INDIAN MEDICAL SERVICE—SECONDED TO THE INDIAN ARMY
MEDICAL CORPS

(Emergency Commission)

(WOMEN'S BRANCH)

To be Captain

Miss Betsy Christiana Zachariah. Dated 21st July, 1944.

To be Lieutenant

Miss Muriel Ellen Lazarus. Dated 6th September, 1944.

PROMOTIONS

The undermentioned General Officer is granted the local rank of Lieutenant-General, without effect on pay and pension :—

Major-General E. W. C. Bradfield, K.C.I.E., O.B.E., I.M.S. (Retd.). Dated 27th October, 1944.

Lieutenant-Colonels to be Colonels

R. A. Logan, O.B.E. Dated 17th July, 1944.

E. Cotter, C.I.E. Dated 30th July, 1944.

The undermentioned is granted the local rank of Colonel (without effect on pay and pension) for so long as he holds the appointment of Honorary Consultant in Psychiatry, Eastern Command :—

Lieutenant-Colonel M. Taylor, O.B.E., Superintendent, European Mental Hospital, Ranchi. Dated 28th September, 1944.

The undermentioned officer is granted the local rank of Colonel without effect on pay and pension with effect from 21st September, 1944, whilst employed as Assistant Director of Malariology, Medical Directorate, G.H.Q.(I.) :—

Major (temporary Lieutenant-Colonel) W. B. Stiver, seconded to I.A.M.C.

Major to be Lieutenant-Colonel

W. Scott. Dated 3rd September, 1944.

Captains to be Majors

1st November, 1944

D. J. P. Parker. T. C. M. M. Morrison.

Lieutenant to be Captain

J. M. Mungavin. Dated 11th May, 1942.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commission)

Lieutenants to be Captains

M. L. Barma. Dated 12th July, 1944.

15th July, 1944

M. M. Roy. S. Ganguly.

J. P. Shrivastava.

S. A. A. Sami. Dated 24th July, 1944.

N. B. Thandani. Dated 15th August, 1944.

S. S. Zoha. Dated 20th August, 1944.

H. R. Varadarajan. Dated 30th August, 1944.

H. Chand. Dated 15th September, 1944.

(WOMEN'S BRANCH)

Miss C. Sarojini. Dated 15th October, 1944.

INDIAN AIR FORCE—MEDICAL BRANCH
Flying Officers to be War Substantive
Flight-Lieutenants

F. V. Tawadey. Dated 24th January, 1944.

D. N. Gupta. Dated 3rd July, 1944.

4th July, 1944

B. Bhatia.

V. B. Kalra.

H. S. Seth.

RELINQUISHMENTS

The undermentioned officer is permitted to relinquish his commission and is granted the honorary rank of Major :—

INDIAN MEDICAL SERVICE

SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commission)

Major E. D. Anklesaria. Dated 1st September, 1944.

The undermentioned officers are permitted to relinquish their commissions on grounds of ill-health, and are granted the honorary rank of Captains.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commission)

Captain Mandula Anantasayanam. Dated 20th October, 1944.

25th October, 1944

Captain Nurur Rahman.

Captain Krishna Chandra Mukherji.

Captain Koka Dattatreya.

Captain Syed Zahiruddin Ahmed. Dated 1st November, 1944.

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Original Articles

SUBACUTE CONSTRICTIVE PERICARDITIS

By R. VISWANATHAN, B.A., M.D., M.R.C.P. (Lond.),
T.D.D. (Wales)

LIEUTENANT-COLONEL, I.A.M.C.

*Officer Commanding, Medical Division of an Indian
General Hospital*

THE two cases described below presented the typical pathological picture of constrictive pericarditis; but the clinical course in both cases was so short that the nature of the disease was not recognized at the beginning. As both cases had a fatal termination within five months of the onset of the first symptoms, I choose to call them subacute constrictive pericarditis. A remarkable feature in both cases was the tuberculous origin and its nature, the pericardium being primarily affected without any tuberculous lesion in any other part of the body except in one solitary gland in the hilum.

Historical.—Lower was the first to give a satisfactory description of pericardial disease. Clinical recognition of constrictive pericarditis was made by him. From then on for a period of 100 years, a series of cases was reported by Bonetus, Vieussens, Lancisi and Morgagni (White, 1935). Then for a century following the observation made by Laennec (White, 1935) that adherent pericardium may exist without symptoms or signs, little mention of the subject was made until Pick (1896) published his paper entitled 'Concerning chronic pericarditis running its course under the guise of cirrhosis of the liver (pericarditic pseudo-cirrhosis of the liver).' Though before Pick's time in the nineteenth century four other physicians, Griesinger (White, 1935), Kussmaul (1873), Chevers (1842) and Wilks (1870), had made important observations on the subject, it was only subsequent to Pick's paper that clinical recognition of the disease became more frequent, and successful surgical treatment was adopted. Weill (White, 1935) and Delorme (1898) were the first to suggest pericardial resection for constrictive pericarditis. But it was left to Rehn (1920) and Sauerbruch (1925) to perform the first operations. One of the best contributions to the diagnosis of the condition was made by Volhard and Schmieden in 1923. A review of the subject with good bibliography was made by Schur (1934) of Vienna. Recent American medical literature contains many contributions on the subject from Beck (1931), Burwell and Strayhorn (1932), Churchill (1929), White (1935) and Harrison and White (1942).

Definition.—White defines constrictive pericarditis as a chronic fibrous or callous thickening of the wall of the pericardial sac which is so contracted that the normal diastolic filling

of the heart is prevented, and a condition called 'inflow stasis' results. 'Chronic compression of the heart occurs thereby, and the inflow of the blood during diastole is impeded'. Consequently chronic venous congestion is produced resulting in enlargement of the liver and even ascites.

Etiology.—Practically all writers on the subject are agreed that rheumatism is rarely, perhaps hardly ever, a causative factor in constrictive pericarditis. Lewis (1942) calls it a comparatively rare malady, evidently inflammatory but usually insidious in origin, and rarely attributable to any particular infection. In White's fifteen cases, two were definitely tuberculous in origin and two more were probably tuberculous. The two cases reported here were definitely tuberculous. It is possible that many more cases which are reported to be of unknown origin might have turned out to be tuberculous if histo-pathological examination had been carried out.

Pathology.—Whatever be the cause, dense fibrous thickening of the pericardium occurs. It usually involves both the parietal and the visceral layers. Sometimes there is a chronic mediastinitis involving the pericardium as well as the pleura. The fibrous tissue around the heart is so thick as to be unyielding and of a cartilaginous consistency, sometimes containing calcareous deposits. This produces impediment to the diastolic filling, and embarrassment to the systole of the heart. In some cases, while the pericardium over the apex is free and only slightly thickened, the part over the right auricle and the great veins is markedly contracted. In others, the entire heart and the roots of great vessels (as in the two cases reported below) may be completely encased in a constricting unyielding envelope. The enlargement of the liver first described by Pick in this disease is due to chronic venous congestion resulting from obstruction to the venous return. Firmness of the liver, which led to its being called pseudo-cirrhosis, results from a relative increase in connective tissue, following necrosis of parenchymatous cells.

Symptomatology.—White (1935) describes the first symptoms noticed in his fifteen cases; dyspnoea in four, abdominal enlargement (*i.e.* a big liver and ascites) in three, dyspnoea and abdominal enlargement in three, oedema of the feet and abdominal enlargement in two, oedema of the ankles in one, oedema of the face and abdominal enlargement in one, and soreness in the right upper quadrant in one. In one case reported below, enlargement of the liver was the presenting symptom, while, in the other, dyspnoea was the first symptom noticed.

The signs are mostly those of chronic venous congestion, which results from incomplete expansion of the heart during diastole due to the unyielding pericardium, and also from the actual constriction of the veins. There is conspicuous engorgement of the cervical veins with

or without pulsation. The congestion is out of proportion to the degree of breathlessness and enlargement of heart. The next striking diagnostic sign is the marked enlargement of the liver. Ascites is a common associated finding. Swelling of the legs is less common. In the cases where the superior vena-cava is markedly constricted, swelling of the face is found.

Paradoxical inspiratory swelling of the veins, which is commonly noticed in this disease, is probably due to fibrous bands getting tighter from the great veins during inspiration.

The blood pressure and pulse pressure are as a rule lowered. Paradoxical or Griesinger-Kussmaul pulse is also noted in many cases. During inspiration there is greater interference with the filling of the heart in mediastinopericarditis. Consequently the pulse becomes smaller, and the arterial pressure falls. The apex beat is neither visible nor palpable. Owing to adhesion to the anterior chest wall, there is no variation in the absolute cardiac dullness during respiration.

Radiography usually shows the border of the heart to be straighter than normal. Screening will reveal limitation of diaphragmatic movements near the apex, reduction in pulsation, and immobility of the heart with change of posture.

Electro-cardiographic curves are invariably of low voltage. Changes in the T waves may also be observed.

Diagnosis.—The presence of unusually engorged veins with absence of signs of valvular disease, or cardiac enlargement or marked dyspnoea should make one think of the possibility of constrictive pericarditis. This condition should be borne in mind when one meets with unexplained ascites and enlargement of the liver. Radiography and fluoroscopy will help in arriving at the correct diagnosis.

Constrictive pericarditis may be confused with mitral stenosis, tricuspid valvular disease, cirrhosis of the liver and nutritional or other oedema. One of our cases was originally mistaken for beriberi, while the other was diagnosed primarily as chronic amoebic hepatitis.

Prognosis.—Constrictive pericarditis is ordinarily a chronic malady. It is a disease lasting for many years, producing partial or complete invalidism unless the condition is relieved by surgical treatment. Unlike the cases described by White, the two reported were subacute in their course, and had a fatal termination. Both persons were leading active army life for several months before the onset of the disease. In one, it lasted for four months, and, in the other, five months. The more rapid progression of symptoms made diagnosis difficult in the beginning.

Treatment.—Delorme's (1898) operation of pericardial resection is the only cure for chronic constrictive pericarditis. Operative treatment with good results has been recorded in a number of cases in recent years. After operation, relief

from symptoms is definite and almost immediate, irrespective of the aetiology of the condition.

Case 1.—Hindu, male, aged 21 years, army service two years, was admitted to a general hospital with breathlessness, abdominal swelling and pain in the right hypochondrium of one and a half months' duration. The symptoms were gradually getting worse, though they were not bad enough to prevent the patient's transfer from one hospital to another. On admission to the above hospital, he had a moderate degree of dyspnoea, swelling of the lower limbs, puffiness of the face and engorgement of the neck veins. The apex beat was neither visible nor palpable; pulse was rapid, pulsus alternans; blood pressure 90/55. Liver tender and enlarged to umbilicus; urine clear; radiographically, the borders of the heart were found straightened, the costo-phrenic angles obliterated. Knee jerks absent, slight tenderness of calf muscles. A provisional diagnosis of beriberi was made, and the patient was treated accordingly. There was improvement in the general condition which lasted for a month. Afterwards the patient began to develop ascites and hydrothorax. Enlargement of the liver, ascites and engorgement of veins enabled the diagnosis of constrictive pericarditis to be made. A few days before death, which occurred 10 weeks after admission, the patient developed anasarca, confined mostly to the trunk and lower extremities.

Post mortem.—Oedematous condition of the body except the face and arms. Peritoneum contained four pints of serous fluid. Intestines and omentum oedematous. Liver thrice normal size, hard. When the vena-cava was cut just near the diaphragm, about a pint and half of blood rushed out, and the liver shrank to half the size; cut surface showed typical nutmeg appearance.

Heart.—Pericardium thickened, hard and densely adherent; both the layers intimately adherent throughout. There was marked constriction at the opening of the venæ-cavæ. The chambers of the heart were reduced in size. The myocardium looked apparently healthy.

One hilar gland was found caseous and adherent to the pericardium. Microscopically, typical giant-cell systems characteristic of tuberculous granulation tissue were found in the pericardium (see figure 1, plate III). There was extension of the process in between the myocardial fibres in certain areas adjacent to the pericardium.

Case 2.—A water carrier, aged 28 years, was admitted to an Indian general hospital with diagnosis of asthma and amoebic hepatitis. He had had a full course of emetine and a few adrenalin injections. When first seen by the writer, the patient had a moderate degree of breathlessness but not of the expiratory type. The liver was enlarged to 2 inches below the umbilicus, and hard. The veins of the neck were very prominent even in the sitting posture. The apex beat was not visible; heart boundaries apparently normal; sounds were muffled. Over a small area, a pericardial rub could be heard. Pulse irregular, suggestive of auricular fibrillation. X-ray showed straightening of the borders. Two weeks later, he developed effusion in both pleural cavities. Three months after admission he died.

Post mortem.—Heart small, pericardium densely adherent throughout, thick and hard, cartilaginous in consistency. Histologically, the same appearance as in the first case. The liver had a typical appearance of chronic venous congestion. Lungs normal. Fluid in both pleural cavities. Hilar glands normal except one, which was caseous (see figure 2, plate III). Section revealed its tuberculous nature.

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PLATE III
SUBACUTE CONSTRUCTIVE PERICARDITIS :
R. VISWANATHAN. PAGE 61.

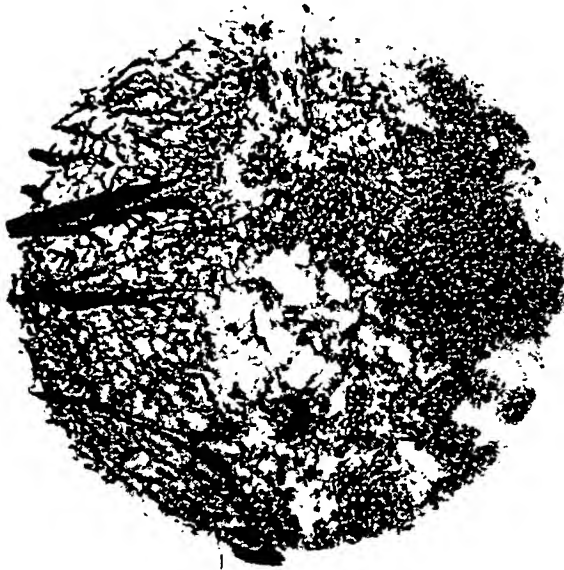


Fig. 1.—*Case 1.* Photomicrograph of section through myo-pericardial junction showing tuberculous infiltration with giant-cell systems.



Fig. 2.—*Case 2.* Section of a hilar gland showing giant-cell system.

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THE DIAGNOSIS OF EARLY GASTRIC CANCER

(WITH A REVIEW OF 60 CASES)

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CANCER of the stomach has received so much attention in recent years that one would naturally expect an appreciable improvement in the 'salvage' rate of patients with malignancy in this region.

Nevertheless, statistics published by various clinics throughout the world fail to bear this out, and greater effort seems called for, if any appreciable improvement is to be achieved in the mortality rate.

The prime factors involved, in the maintenance of the high 'incurability' rate of gastric cancer, are undoubtedly (1) the lack of clinical and other evidence in its incipient stage and (2) the unprogressive nature of whatever slight, apparently irrelevant symptoms are present; which belies the extent and spread of cancer in this viscus.

There is unfortunately a misconception still prevalent, and found in most of the surgical textbooks, that early cancer of the stomach can be diagnosed from signs and symptoms alone. That it cannot be so diagnosed in most cases, must be emphasized. It can only be suspected, and laboratory and clinical aids and x-rays are required, and are indeed essential, in establishing a definite diagnosis. As Moynihan (1928) emphasizes—'there are no symptoms pathognomonic of early cancer of the stomach, the symptoms are suggestive, not conclusive'.

In the stomach, cancer sometimes appears furtively but may develop with shocking suddenness, and with few symptoms may attain extensive dimensions within a short space of time. Thus, for example, there is the small group of patients who can never be saved, because the lesion metastasizes so early, the so-called rapidly metastasizing cancer of Jarco.

In the more specialized clinics in the U.S.A. and Europe, immediate x-ray and laboratory aids and gastroscopic examination are requisitioned whenever symptoms relating to the gastro-intestinal tract are present for even single month.

The first great problem of gastric cancer, therefore, is public education. The second and equally difficult problem for which the general practitioner is undoubtedly responsible, is early diagnosis; as most of the patients go to him for primary relief. This early diagnosis as already stressed, is only possible if the average general practitioner is constantly cancer conscious. 'Eternal vigilance is the price of safety.' It must be fully realized that to await the classical symptoms of cancer of the stomach is to await certain death. The post-mortem appearances of a fatal case with a history of increasing epigastric lump, cachectic and dehydrated, must be dismissed from our minds. We must picture our gastric patient as a well nourished apparently healthy individual who comes to a doctor because he feels that he is not keeping quite fit. His sleep is disturbed; he is less energetic than he was; he is aware of malaise. Indeed he is more likely to realize that he is not perfectly well than to think that he is ill. He may deny gastric disturbances entirely, and think that all he needs is a tonic. Nine times out of ten he is past forty. A gastro-intestinal x-ray series may prove expensive, but may save his life.

In 1940, Pack and Livingstone extensively reviewed world literature dealing with treatment of cancer of the stomach, and sought to come to a conclusion on certain matters. The main points they wished to clear up were: (1) the percentage of applicability of gastrectomy in the total number of cases submitted to surgery, (2) the risks involved in this extirpation of the cancer and (3) the effective results achieved when a gastrectomy is successfully performed.

They found the following state of affairs:—

Of every 100 patients with gastric cancer in the average American hospital, 50 per cent are found from the first in an inoperable condition and have to be discarded without any hope of salvage. This is the first loss factor. Of the remaining 50 who undergo a laparotomy, barely 25 are found resectable, so that the remaining 25 have no chance of a 'cure', though palliative measures like gastro-jejunostomy can indeed be undertaken. This we may call the second loss factor. Finally of the lucky 25 undergoing gastrectomy, 20 per cent, or 5 patients, do not survive the operation—this being the average resection mortality in America to-day. And this is not all; of the 20 patients who survive this acid test, two-thirds die within 3 years, three-fourths within 5 years and four-fifths by the end of the 10th year. This is then the final loss factor.

Thus we have at the end only 3 to 6 definite cures of the 100 patients originally seen.

Very correctly however Pack and Livingstone state that they assume two points of view with regard to the curability of gastric cancer. 'A pessimistic view of the disease as

a whole, with only 3 to 6 per cent cures of the total patients seen, and an optimistic outlook of 20 to 30 per cent five-year survivals without recurrence, for those patients with resectable gastric cancers¹.

agents. It has no distinctive features to differentiate it from the indigestion of other origin. A guess is the best that a clinician can offer in about 25 per cent of early cases of gastric cancer; and a guess, as Lord Moynihan aptly

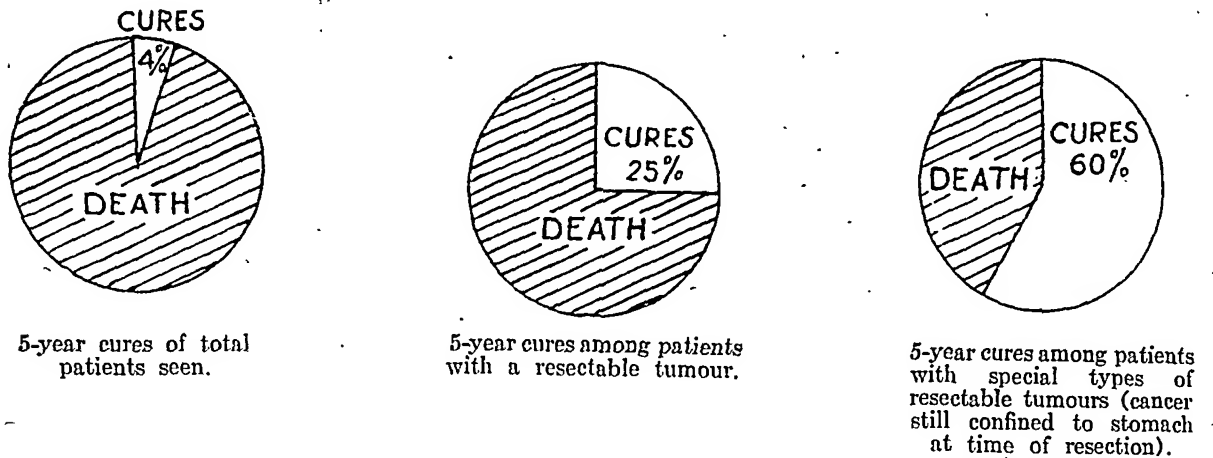


Fig. 1.—Graphic presentation of prognosis for patients with different types of gastric cancer. (Pack and Livingstone.)

Walters, Gray and Priestley (1943) from the Mayo Foundation in reporting on their figures for the years 1907 to 1938, mention that 58 per cent of the total number of patients with malignant lesion of the stomach were considered operable (the first loss factor being 42 per cent), but that in only 45 per cent of these was the lesion resectable (the second loss factor being 32 per cent of the whole group). This leaves us with 26 per cent of the original group observed. Of these 26 per cent, 16 per cent died in hospital as a result of the operation, leaving us with 22 per cent of the total number seen. (In 1940, the mortality rate for resection was brought down to 8.8 per cent, leaving us with 24 per cent cases only.)

Thus even with gastric surgeons as capable as Walters, Gray and Priestley (1943), paradoxically enough no great increase in the number of gastric cancer cures occurs, because the difference in resection mortality of 10 per cent and 25 per cent means the saving of only 3 to 5 more patients of the 100 originally seen. This is so because operative skill can improve only the figures for resectability of the tumour, and the operative mortality; but is unfortunately restricted in its application to the 25 to 33 per cent of patients with technically resectable cancers. The rest of the 67 to 75 per cent of cases can be saved only to a certain extent by the general practitioner who stands here at the cross-roads directing the stricken either to safety or to nemesis and destruction. It is he alone who can reduce this carnage of the first loss factor. Gastric cancer more often than not taken on the garb of benignancy and innocence in the early months of its existence, and the indigestion caused by it in the early stages is identical with that caused by various other

puts it, is a poor peg to hang a man's life upon.

As every physician knows, though as not all physicians remember, there are at least a dozen different clinical syndromes of early gastric cancer. Each one of these may lead the diagnostician astray, and the first and second loss factors of from 67 to 75 per cent are grave reminders urging the physician to make a freer use of the various diagnostic aids available, before excluding cancer in this viscus. Stomach cancer is a surgical disease from the start, and as such should never be treated medically.

Out of the first 7,000 cases seen at the Tata Memorial Hospital* only about 5,000 were cases of cancer. A diagnosis of carcinoma of the stomach was made in only 60 of these cases, giving a percentage of roughly one per cent of all cases seen at the hospital. These figures are much below those reported by others, especially from the west, and are not indicative of the true state of affairs as most of our cases are referred to us by doctors outside.

Of these 60 cases, the lesions in 26 were either inoperable, and the individuals merely received palliative medical treatment; or the patients refused operation on the advice of their family physician. This makes a clean sweep of 44 per cent of the total cases seen, leaving us with only 56 per cent of the original group. This is our first loss factor. This is the group from amongst whom we should be able to save a fair percentage. It is the aim of this paper to find ways and means to accomplish this object.

The remaining 56 per cent or 34 patients underwent an exploratory operation in the hope that

* This hospital exists for the purpose of studying tumours, so the proportion of cancer cases is very high.

a gastric resection might be accomplished. Among this group, there were 8 inoperable cases, and in each of these the incision was closed and nothing further attempted. Thus another 14 per cent of the entire group was swept off the board. In an additional group of 8 cases, the lesion could not be surgically removed, but yet some form of palliative procedure was undertaken to by-pass the obstruction, so that a further 13 per cent of the total number of cases was lost as none of these can be claimed as 'cures'. This leaves us finally with 18 cases (30 per cent) only, wherein a radical gastrectomy was accomplished. These 18 cases out of the total group of 60 were given a chance of cure; in other words, only 1 in 3 was offered radical treatment, and provided the patient survived the surgery, a sneaking chance of future existence.

In an additional group of 14 cases, gastrectomy was performed on account of a suspicious x-ray appearance and clinical picture, but on pathological examination these turned to be non-cancerous. This series is not included in the present report. There was no death in this group.

The surgical rate of gastric cancer thus works out to be 56 per cent and the resectability rate 30 per cent, of the total number of patients seen here. More encouraging figures are obtained if the resectability rate is calculated only from amongst those cases in which an operation in some form or another was performed; of 34 such cases the resectability rate works out to be 53 per cent.

The operative mortality rate in this series for all types of gastric resection for cancer was 27 per cent, including 3 cases of total gastrectomy. If only cases of subtotal gastrectomy are taken, the mortality drops to 18 per cent. In the last 6 months, 7 more cases were 'gastrectomized' with an improved mortality of 14 per cent, only one case being lost. These cases are not included in this report. No five-year survivals are being

Of these 60 cases of gastric cancer, 40 victims were claimed from the male sex and 20 from the female, thus giving a ratio of 2 to 1 against the men. However, this ratio is roughly identical with that for general attendance at the hospital, so if the figures are corrected for attendance, cancer of the stomach can be said to have claimed an equal proportion of males and females. The youngest individual of the series was a woman of 26, the youngest man thus afflicted being 27. The oldest was also a woman 74 years of age. The oldest man was 73. The average age in men was 55 and in women 53.

Grading of cases was done according to Broders' method. The pathological grading of cases in which a gastrectomy was done showed that the majority were of high malignancy, grade 3 predominating. Nine were grade 3; five were grade 2; two were grade 1 and two were grade 4, the most malignant. Out of these 18, both patients of grade 4 are already dead; six of grade 3 are alive and well; four of the 5 with grade 2 lesions and both the grade 1 cases are well. This shows that cancer of the stomach falls in line with carcinoma elsewhere, the higher grade being more malignant and claiming more victims.

We have thus a gloomy picture before us, which amply justifies a constant repetition of the difficulties that may prevent early diagnosis of gastric carcinoma.

Within the last 10 years or so, a great improvement has been achieved in the operative mortality of radical gastrectomy especially when performed by a group of men working as a team in a hospital where special facilities are obtainable and ready at hand. This has been the experience even in a rich country like the U.S.A. where, generally speaking, no lack of funds is seen. This is clearly demonstrated by Pack and Livingstone (1940), and will be dealt with at greater length in a subsequent article by us.

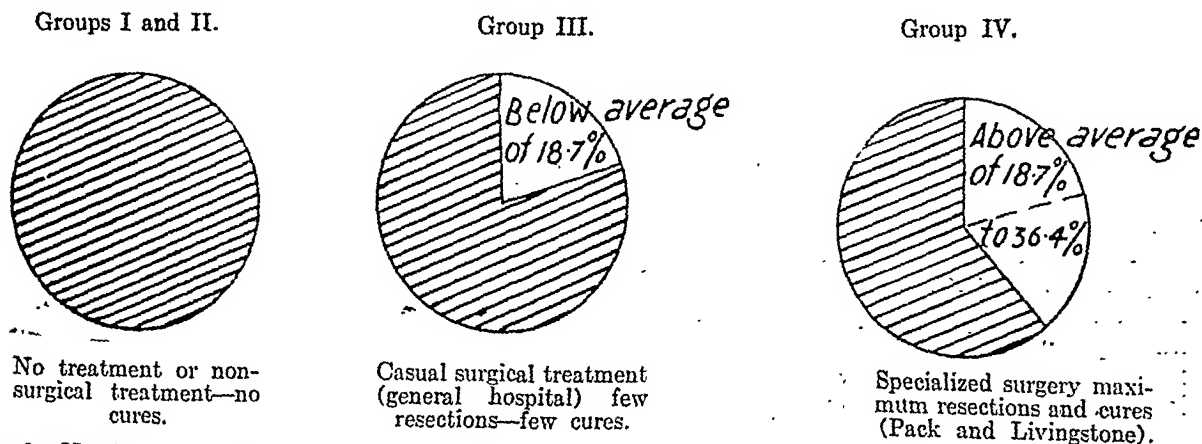


Fig. 2.—Number of patients undergoing gastrectomy for cancer in the U.S.A. as a whole. A study of general conditions as contrasted to those in special clinics.

claimed so far, because this hospital itself has yet to celebrate 5 years of its existence.

Nowadays the mortality of subtotal gastrectomy has been brought down to a respectable

level in such specialized institutions, and this should encourage the patient as well as the general practitioner to entrust the case for radical surgery to a reputed specialist. It has been our unfortunate experience in some cases to find a patient with an early cancer refusing surgery merely because the family physician has impressed on him that under no circumstances should he consent to an operation. There are no two opinions to-day with regard to treatment of gastric cancer. To choose between an ultimate 100 per cent mortality of medical or other treatment and the 10 per cent or 15 per cent operational mortality of radical surgery with some hope of radical cure should not be difficult. The nineteenth century ideas regarding mortality of a gastric resection should find no place with us to-day. Till very lately, St. John reported a mortality of 43 per cent, Oughterson 52 per cent, and Maes and Boyce from New Orleans 51 per cent. However, with greater experience, more facilities and better team work, Balfour has reported a mortality of 5 per cent, and Yudine of Moscow 6 per cent.

Going into the symptomatology of these cases we find that they can be readily divided into three broad groups:—

1. The first group includes patients who complain of vague ill-health. No gastro-intestinal symptoms appear, and when the individual finally lands on the physician's door-step, he is already beyond help. An occasional case here and there may come early enough, but as a rule the root cause of all his troubles is missed. An astute practitioner should promptly investigate the gastro-intestinal tract of any patient at or beyond middle age who complains of failing health for the first time and shows no apparent cause for these symptoms. In this group, the chances of cure will remain remote until physicians in general bear this factor always in mind. Most cases from this group unfortunately seek medical aid very late, as they have no distressing symptoms to complain of, and have been in excellent health all their lives. As a rule, they are very proud of their digestive abilities, and proclaim themselves to be gastronomical athletes like Napoleon. Unfortunately, like that historical hero, they die of cancer of the stomach.

2. The second group includes those cases in which debility and easy fatigue are associated at the outset with vague and ill-defined symptoms of dyspepsia. Patients of this group often complain of being martyrs to indigestion, and dope themselves with 'dinner pills' and patent medicines galore, insulting both their digestion and other metabolic processes with fashionable diets, 'internal' baths and frequent bowel washes till they are well past the curable stage of this disease. The chances of cure are better in this group than in the first, but yet not promising enough, chiefly because, though diagnosis is not completely obscured and rendered

difficult to make, it is seldom made within the first six months of the onset of symptoms.

3. The third group which is unfortunately the smallest includes those individuals who have a definite history of gastric or duodenal ulcer for a period of months or years before the malignant character of the lesion is recognized. Their symptoms are definitely acute enough to direct the attention of the attending physician to the stomach. Unfortunately even this does not save the patient many a time. He is treated as a case of peptic ulcer, and no care is taken to insist on x-ray examination of the gastro-intestinal tract. Some more unfortunate patients even have an x-ray plate taken, but the early malignant changes in the ulcer are not correctly interpreted.

It will not be out of place here to stress once again that to exclude cancer of the stomach the surgeon or the radiologist should under no circumstances take the amount of gastric acidity as a guide in coming to a diagnosis. In the presence of even a small filling defect in the gastro-intestinal series, a diagnosis of cancer of the stomach should be made, rather than excluded on the basis of a hyperacidity. It is much wiser to gastrectomize a few suspicious cases of gastric ulcer than to delay a radical operation even in one case of early cancer of the stomach. After all, a subtotal gastrectomy is the best treatment for a gastric ulcer, and the operative mortality of this operation for non-cancerous cases in good general health is never more than 5 to 7 per cent, at the most. Certainly, if possible, further x-ray studies should be undertaken and the mucosal pattern thoroughly examined. Also whenever possible, a gastroscopical examination and biopsy should always be done. However, in those cases where these additional examinations cannot be undertaken, we may stress once again that a gastrectomy is always the wiser and safer course to follow. It may seem that we are giving undue importance to this factor, but we have had cases where exactly this mistake has been made, and the patient has been referred very late. In a few cases, the original x-ray picture was wisely taken early enough, but was misinterpreted in a most unwise manner, chiefly because the radiologist based his diagnosis on the gastric hyperacidity rather than on the x-ray appearance; and the surgeon or physician did not dare to differ from the radiologist. We may cite the following case to bear out this statement:—

Case no. 447, T.M.H.—A 45-year-old Hindu female sought relief from epigastric pain of 2 years' duration. The onset of pain was within one hour of taking food, and only occasionally followed by vomiting, with relief of pain. She consulted a doctor who prescribed some tablets for her. She felt a little better, but was never completely without pain. Two months later she again became worse, and this time the pains were more severe and of longer duration. A gastric analysis was done and hyperacidity was found. This fact apparently caused the physician to rule out cancer of the stomach. She was given some more medical treatment but as she did not feel better she herself came to this hospital

for help. We found a very emaciated woman of middle age with no positive findings except for a vague tenderness and some muscle guarding in the epigastrium. Gastric analysis revealed a free acidity of 164 and a total acidity of 184. The gastro-intestinal series done elsewhere revealed a slight filling defect at the pylorus which suggested early malignant change. This finding was missed outside. An operation was immediately indicated but the patient did not consent to this till two months later. This time the x-ray appearance did not leave any doubt as to the diagnosis. After the usual pre-operative preparation she was opened up and a subtotal gastrectomy performed successfully. The patient never recovered from secondary shock and died on the 4th post-operative day. At the time of the operation she was reduced to a mere skeleton weighing only 70 lb. and could hardly stand without help. Her blood pressure was 60-40. An operation was indicated because of marked obstructive features. On the table the tumour was quite free and movable and a chance was taken with a more radical procedure than was at first contemplated because of the absence of technical difficulties. Had she consented to an operation when it was first suggested she would have had an excellent chance of radical cure.

The next case illustrated the futility of treating the so-called peptic ulcers without x-ray examinations.

Case no. 5742, T.M.H.—The patient was himself a medical practitioner, aged 53. He complained of epigastric pain after food, which had been present for one year when he came to us. The pain used to occur 2 hours after a meal just to the right of the midline in the epigastrium. He felt relieved on taking Cal-Bisma powders. His general condition was however deteriorating, so he came to Bombay for a consultation. He was seen by a physician who confirmed his diagnosis of 'peptic' ulcer, gave him 'Larostidin' injections and told him not to worry about his condition. He felt better for some time afterwards but when he felt food apparently sticking at the level of the lower end of the sternum he came to us for help. A gastro-intestinal series at once revealed a very extensive cancer involving the lesser curvature and extending up into the oesophagus. No surgery could be contemplated because of the extent of the lesion.

Very correctly, Moynihan lamented the fact that 'the success of medical treatment in early cases of cancer of the stomach is one of the causes of high mortality from the disease'.

We can cite many more patients in whom a typical history of peptic ulcer was obtained in the early period of the disease, who improved on medical treatment but later on were found to have gastric carcinoma. Thorough examination at this early stage might have revealed the malignant character of the lesion.

Sometimes the stomach-cancer victim falls into the hands of an 'appendicitis' surgeon, who removes the appendix never suspecting a gastric cancer.

Rives (1939) has reported such symptoms in 50 out of 200 cases of proven gastric cancer, Saur in 32 out of 220 cases, Woolsey in 18 out of 100 cases, Walton in 44 out of 461, and Alvarez in 51 per cent of 41 cases.

Amongst our cases, a typical history of gastric or duodenal ulcer was obtained in no less than 35 per cent of patients with gastric cancer; this figure is much higher than that reported by most others. This suggests that our problem in this country is to some extent easier to tackle than

elsewhere, because our attention is drawn to the gastro-intestinal tract, and we do not have to deal with so many 'silent' cancers.

Doubtless the diagnosis of gastric or duodenal ulcer should have been made in these cases early in the course of the disease. But those cases which did not respond to medical treatment promptly, with a 'complete' amelioration of the symptoms, should have been x-rayed, and at the least suspicion of malignancy, should have been operated upon. The mortality in the hands of an experienced surgeon is not at all prohibitive. Even if the lesion turns out to be of a benign nature, a subtotal gastrectomy is nowadays the accepted treatment for such conditions, and furthermore the operative mortality in non-cancerous lesions has been found to be lower than in cancer.

A number of excellent clinical criteria have been laid down by Lahey *et al.* (1935) and Jordan (1939), by Scott, by Rives (1939) and others to minimize the delay in the treatment of these cases. We have outlined a plan along those lines.

1. Medical treatment should be employed in cases with symptoms of gastric and duodenal ulcer only after x-ray examination has ruled out cancer of the stomach. This treatment should be very stringent and carefully controlled by the physician.

2. If x-ray examination cannot be undertaken for any reason, medical treatment should not be persisted with for more than 3 to 4 weeks if the symptoms are not completely controlled. Radical surgery should be instituted at once.

3. If the symptoms are controlled by medical treatment but yet the ulcer shows no signs of healing on the x-ray plate, radical surgery should be resorted to. The criteria of healing should be very strict.

(i) The crater must disappear.

(ii) Peristaltic waves must pass freely through the area formerly occupied by the ulcer.

4. Large ulcers with a loss of weight and with or without a low gastric acidity should be treated as carcinomatous in spite of the absence of evidence on the x-ray plate.

These criteria may seem to be rather strict, but in view of the results achieved so far by other means, this seems to be the best and only way by which early cancer of the stomach will reach the hands of those capable of treating it radically. It must never be lost sight of that a radical gastrectomy is the one and only way of treating cancer of the stomach to achieve a cure in a fair percentage of cases.

A few of the more important radiological signs are listed below:—

1. Filling defects are probably the most important.

2. Altered pyloric function, which includes a gaping of the pylorus or an obstruction in that region.

3. An alteration in the peristalsis either hypermotility (rarely), or an absence of peristalsis from the involved area, or yet again an anti-peristalsis in obstructed cases.

4. Loss of flexibility on palpation during screening.

5. Diminution in size of the stomach as in linitis plastica.

6. A niche in the pre-pyloric region as pointed out by Hampton and Holmes of Boston. In 90 per cent of such cases, they found carcinoma of the stomach.

7. A widening of the space between the cardia and the top of the diaphragm (Holmes).

8. A niche along the greater curvature should always be suspected as being carcinomatous.

9. Kirklin's halo sign. The niche is seen on the lesser curvature. On upward pressure, a blank space is noted between the barium filling the crater and the rest of the stomach. This is due to a loss of the rugae in the immediate vicinity of the carcinomatous ulcer.

10. Absence of rugal markings as made out with a small amount of barium, on compression of the stomach under screening, and on the x-ray plate.

These are amongst the more important signs which help in diagnosing a cancer of the stomach.

Conclusions

Symptoms of early cancer of the stomach are very trivial, and the usual textbook picture is found only in advanced cases due to secondary infection, and obstruction. By this time, the patient has lost his chance of cure. 'The only hand that paints a perfect pathological picture is the hand of death.'

We must diagnose gastric cancer before definite symptoms arise. 'Just a little indigestion' in a middle-aged man or woman seen for the first time with a previously healthy digestion should always be fully investigated along these lines, and when in doubt, an exploratory laparotomy is clearly indicated. 'Just a little cancer' usually starts as 'just a little indigestion'. Cancer-mindedness is the only straight and narrow path to an early diagnosis.

Usually before pain arises, the patient complains of abdominal discomfort. He or she is not able to locate the area as in a peptic ulcer, but will often place the hand over the upper abdomen saying that his trouble is under the hand. 'Gas' is said to be the cause of his symptoms, and the clever ones complain of 'gas-tritis'.

Periodicity of the discomfort and apparent improvement with medical treatment do not exclude cancer of the stomach, which often masquerades or starts as a peptic ulcer. A hyperchlorhydria is not an uncommon finding early in the disease. Whatever the percentage of transition of benign into malignant ulceration of the stomach, there is no doubt that some cases do undergo this dreaded change.

X-ray investigations should never be omitted in these cases. A careful interpretation of these findings is of the utmost importance. An expert radiologist is an important and essential member of the specialist team undertaking treatment of gastric cancer.

At the first suspicion of cancer of the stomach, an exploratory laparotomy and radical surgery, if necessary, should be carried out.

We shall close by quoting one of the late Mayos, 'Cancer, cure or console; to cure sometimes, alleviate often, comfort always', the best we can ever hope to do.

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NUTRITIONAL DIARRHŒA

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CASES of chronic diarrhœa are common in South Indian hospitals. In a proportion of these, the etiology is clear; for example, they may be due to tuberculous enteritis or chronic amœbiasis. But when cases of known causation have been excluded, there remains a large group of obscure etiology. Patients in this group belong in general to the poorest classes, and are in a state of malnutrition. Microscopic examination of the stools yields negative results. They are usually treated with a fluid diet and astringents; hydrochloric acid may be given in some instances. Such treatment may lead to some amelioration, but is on the whole unsatisfactory.

The suspicion that defective diet can *per se* produce gastro-intestinal disorders including diarrhœa is justified by a number of recorded observations. McCarrison (1921), working in Coonoor, produced a lethal diarrhœa in monkeys by feeding them on autoclaved rice diets. He

concluded that 'the health of the gastrointestinal tract is dependent on an adequate provision of accessory food factors' and further that 'experiments with animals lead us to expect that acute intestinal disorders will be among the commonest of the consequences of deficient or ill-balanced food'. A number of other workers have observed diarrhoea in monkeys, pigs and other experimental animals fed on diets deficient in various vitamins. McKenzie (1940) described a condition in labourers in East Africa which he called 'nutritional diarrhoea'. He noticed that the incidence of the disease among estate labourers fell remarkably with an improvement in the diet. Rao (1942) produced in monkeys a chronic diarrhoea, associated with atrophic changes in the small intestines, by feeding the animals on ill-balanced rice diets. The pathological changes observed in the monkeys resembled those observed by McKenzie in human beings. Aykroyd (1942) has drawn attention to the fact that the recorded death rate from 'dysentery and diarrhoea' in the Punjab is usually from one-fourth to one-sixth that of Orissa, Central Provinces and Madras. The Punjab is a wheat-eating province with a relatively high consumption of milk, while in the latter provinces rice is the principal or an important staple, and consumption of milk and protective foods in general is low. Heilig (1943), working in Mysore, has described cases of chronic diarrhoea in malnourished patients which could be benefited by the administration of nicotinic acid.

A high incidence of diarrhoea invariably occurs in victims of famine. Porter (1889) in his interesting book 'The Diseases of the Madras Famine of 1877-78' reported that more than three-quarters of those dying in the famine sheds in Madras were suffering from what he called the 'alvine fluxes', that is, dysentery and diarrhoea. In the early stages of the Bengal famine of 1943, so-called 'famine diarrhoea' was the most formidable problem of medical relief.

Clinical observations

Previous to the present investigation, certain members of the staff of the Stanley Hospital, Madras, had gained the clinical impression that nicotinic acid is of value in chronic diarrhoea occurring without obvious causation in malnourished subjects. A number of medical workers elsewhere in India had gained a similar impression. The observations of Heilig have already been referred to. Poor rice diets have a low content of vitamins of the B₂ group including nicotinic acid. In view of these facts, it was decided to carry out a systematic study of the effect of nicotinic acid on cases of chronic diarrhoea in the Stanley Hospital.

A series of cases of chronic diarrhoea presenting themselves for treatment was investigated. Cases of diarrhoea of known causation, e.g. sprue, chronic amebiasis, tuberculous enteritis, etc.,

were excluded after careful examination. Fifty-four cases of chronic diarrhoea which did not belong to any of the known groups were studied, and their response to nicotinic acid investigated.

The investigation included complete clinical examination, and naked eye, microscopic and cultural examination of the faeces. Fat analysis of the faeces was done in 41 cases. In 42 cases fractional gastric analysis was carried out, this being repeated after treatment with nicotinic acid in 14 cases. Blood examinations were made in 46 cases. Four patients (picked at random) were x-rayed after a barium meal. In order to exclude the possibility of improvement due to rest in bed and change of diet, most patients were kept under observation for 4 days without being given nicotinic acid. During this period, all treatment except placebos such as flavoured water by mouth or distilled water injections was withheld, and the usual hospital fluid diet, consisting mainly of arrowroot congee, was supplied. Little or no improvement was observed under these conditions. Some patients were too ill to justify the withholding of treatment, which, as the investigation proceeded, showed itself to be remarkably effective. These were given nicotinic acid immediately on admission.

The fifty-four cases presented well-marked and uniform signs and symptoms. The condition from which they were suffering, to which the not very satisfactory name 'nutritional diarrhoea' has been given, deserves recognition as a specific clinical entity.

Incidence

The patients belonged to the poorest classes. Only 3 cases in the series had monthly incomes per family of over Rs. 25. Thirty-one patients were living on monthly incomes ranging between Rs. 10 and Rs. 25. All the patients were rice-eaters, and prior to the onset of diarrhoea, were mostly living on rice and vegetables without milk, meat or eggs. The majority of patients were middle-aged; 43 were between 25 and 50 years, 3 were below 25 and 8 above 50; the youngest was a child of 12 and the oldest a woman of 68. The great majority of patients belonged to the female sex; 43 patients of the series were females and 11 were males. It must of course be observed that the age and sex incidence of a disease in a group of hospital patients does not necessarily correspond with its age and sex distribution in the general population.

TABLE I
Incidence according to age and sex

Sex	Below 10	10-20	20-30	30-40	40-50	Over 50
Males ..	0	0	3	5	2	2
Females ..	0	3	10	16	7	6

TABLE II
Incidence according to family income

Below Rs. 10 p.m.	Between Rs. 10 and 20	Between Rs. 20 and 30	Above Rs. 30
31	16	5	2

Symptoms

The onset of the disease was usually gradual. In 4 cases there was a history of some protracted febrile illness preceding the attack; in 3 others the disease followed on childbirth. In the rest of the cases, however, there was no history of such precipitating episodes. In the class of patient concerned, clear histories are of course difficult to obtain. The disease started with the patient passing one or two loose stools after food. As it progressed the number of motions gradually increased until, in a severe case, nearly a dozen motions might be passed in a day. Passage of motions was not associated with tenesmus. Abdominal pain and griping were absent, but vague abdominal discomfort was present in all cases. The patients often complained of gurgling noises in the abdomen. Soreness of the tongue, with inability to take hot spicy foods, was complained of by 49 patients at the time of admission; according to these patients the soreness became evident at about the same time as, or a short while before, the diarrhoea started. Twenty-five patients complained of swelling of the lower extremities; these cases had had diarrhoea for over two months when the swelling first started. The swelling was first noticed in the feet and gradually extended upward. The patients in general complained of weakness and inability to make an effort, but no history of mental change was elicited from patients or their relatives.

Signs

All patients showed varying degrees of emaciation. Oedema of the dependent parts was present in 25 cases. The oedema was of the soft-pitting, quick-filling type and shifted with the position of the patient, being always maximum in the dependent parts. The face was involved in only 2 cases. In 15 patients, the skin over the anterior and outer aspects of the legs showed a dermatosis of the 'crazy-pavement' type described by Nicholls (1940), with patches of epithelium of a darker colour than normal separated by fine and irregular fissures. In 2 of these the outer aspects of the forearms were also involved. The hands, face and neck showed no involvement. There was no itching or sensation of burning associated with this skin condition which was very different from the well-marked pigmented hyperkeratosis of the skin characteristic of pellagra. In the course of the investigation only one case was observed which presented dermatitis typical of pellagra on the

extremities, with symmetrical dermatitis of the skin of the cheeks. The skin lesions in this case were not severe and subsided on treatment with nicotinic acid.

Forty-nine patients presented evidence of glossitis. Three main types of tongue lesions were observed: a hypertrophic type with the fungiform and filiform papillae, red and prominent; an atrophic type with the papillae ironed out and the tongue red and smooth; and a fissured type with the tongue showing atrophic changes and traversed by a number of longitudinal and transverse fissures. Combinations of these types were also seen. The hypertrophic type was more common in the early cases with diarrhoea of less than four weeks' duration, while the other types were more frequently present in the advanced and chronic cases. Other evidence of malnutrition was present in a few cases. Eight patients showed angular stomatitis; and one complained of night-blindness. Advanced xerosis was observed in only one patient, but muddy discoloration of the conjunctiva was present in most cases.

Examination of the abdomen revealed slight fullness but no lumps or tenderness in any of the quadrants. The heart, lungs, nervous system and mental state were all normal. A hæmic bruit over the precordium was common.

The motions were loose, and yellow or greenish yellow in colour. They were not foul and frothy, like the motions in sprue. Blood was absent. Mucus was absent except in 8 cases in which traces were present. Microscopic examination showed no amœbæ, cellular exudate or fat globules. Culture of the motions was negative for pathogenic organisms. Fat analysis of the motions invariably revealed a 'low normal' fat content (below 12 per cent) which contrasted significantly with the high fat content (over 45 per cent) of the faeces of sprue cases observed in the course of the investigation.

The patients presented varying degrees of anæmia, the anæmia being of the hypochromic type with colour index less than 1 in 43 cases, and of the macrocytic hyperchromic type in 3 cases. The leucocyte count and differential white cell count, which were done in a few cases, were normal.

Gastric analysis after a test meal, which was carried out in 42 cases, showed total lack of free hydrochloric acid in the stomach in 28 cases, hypochlorhydria in 13 cases, and normal acidity in one case. The response in 5 cases of achlorhydria to histamine injection was studied. In 3 cases the achlorhydria was found to be histamine-fast; in the 2 others a slight response to histamine injection was obtained.

Radiographic examination after a barium meal in 4 cases revealed marked hypermotility of the stomach, small intestine and large intestine. Thus, in one case, the barium had left the stomach in 5 minutes, reached the ileo-cæcal junction in 30 minutes, and the rectum in the fourth hour.

TABLE III
Clinical data

Signs	Number of cases
DIARRHOEA	54
Less than 6 motions a day	13
Over 6 motions a day	41
With mucus	8
Without mucus	46
Of less than 2 months' duration ..	10
Between 2 to 6 months' duration ..	31
Over 6 months' duration	13
GLOSSITIS	+ 49
Hypertrophic type	- 5
Cases of this type of less than 2 months' duration.	13
Cases of this type of over 2 months' duration.	9
Atrophic and fissured types	4
Cases of this type of less than 2 months	36
Cases of this type of over 2 months ..	1
EDEMA	35
Cases of oedema with diarrhoea less than 2 months.	+ 25
Cases of oedema with diarrhoea over 2 months.	- 29
'CRAZY PAVEMENT' DERMATOSIS ..	0
ANÆMIA—	+ 15
Number investigated	- 39
Microcytic hypochromic	46
Macrocytic hyperchromic	43
GASTRIC ACIDITY—	3
Number investigated	42
Achlorhydria	28
Hypochlorhydria	13
Normal	1

Response to nicotinic acid

A striking response to the administration of nicotinic acid was obtained in 50 cases. In severe cases, 100 mg. of nicotinic acid were injected intramuscularly daily. In milder cases, 50 to 75 mg. a day were given according to the severity of the case. Improvement was usually apparent after the third injection. The motions were reduced in number, and became more formed. Patients who passed over 10 loose motions before treatment was begun usually had only 4 semi-solid motions after the third injection. The diarrhoea was controlled within 12 days in all 50 cases, the patient thereafter passing only one formed motion a day.

Four cases failed to respond to the administration of nicotinic acid. These were highly advanced and chronic cases in patients who had had diarrhoea for over 6 months before coming into hospital. They were admitted in a state of gross emaciation with severe oedema. Injections of 100 to 150 mg. of nicotinic acid intramuscularly daily did not cause any improvement. Their general condition deteriorated steadily. Three cases died within 10 days of admission into hospital, and one case was removed home in a moribund state.

Parenteral administration of nicotinic acid gave better results than oral administration, and in severe cases, the former seems necessary to obtain satisfactory results. In 5 cases of a severe type, no improvement was observed after giving 300 mg. of nicotinic acid by mouth daily for 4 days. A striking response was, however, obtained in these cases when 100 mg. daily were administered intramuscularly. In the milder cases, with 3 or 4 motions in the course of 24 hours, for which 50 mg. by the parenteral route is a suitable dose, 300 mg. by mouth yielded equally good results. In practice, it was found that in severe cases the injection of 100 mg. daily for 4 or 5 days until the motions were reduced in number to 3 or 4 in 24 hours and were becoming formed, and the oral administration of 300 mg. daily for 5 to 7 more days, gave satisfactory results.

Administration of nicotinic acid had no immediately beneficial effect on the oedema. The immediate result of controlling the diarrhoea was often to worsen the oedema. When the patient, after improvement in the diarrhoea, was put on the full hospital diet, the oedema gradually disappeared. Presumably the cessation of the diarrhoea removed a channel of fluid elimination and tended at first to make the oedema worse. It was noted that injections of thiamin had little effect on the oedema, which is probably the result of hypoproteinaemia induced partly by diarrhoea and partly by dietary deficiency. A low serum protein level was found in two cases with oedema, but in this investigation the problem of the causation of oedema was not specifically studied.

The feeling of soreness of the tongue diminished during treatment. Patients who on admission were unable to tolerate spicy foods were able to take the full diet of the hospital after treatment, with little discomfort. The glossitis showed varying degrees of improvement after treatment, but in no case did the tongue regain a completely normal appearance. In cases showing the 'crazy pavement' dermatosis no striking change in the skin condition was noticed.

Repetition of the fractional gastric analysis in 14 cases after nicotinic acid treatment did not reveal any change. The achlorhydria or hypochlorhydria persisted. Radiographic examination after a barium meal, repeated after treatment in one case, showed a return of intestinal motility to normal, or almost to normal. In this case after treatment, the head of the barium meal reached the ileo-caecal junction in the fifth hour.

Recurrence

Eleven cases re-appeared in hospital within two months of their discharge with recurrence of diarrhoea; these were again treated with nicotinic acid and showed the same striking improvement. No doubt on discharge from hospital they returned to the same inadequate diet as they had

consumed previous to admission. It appears that a maintenance dose of nicotinic acid, or a general improvement in the diet, is necessary to prevent recurrence.

Typical case records

1. Patient B., female, 30 years. Admitted on 21st September, 1943, with diarrhoea of 6 months' duration, passing 10 loose motions a day without blood or mucus. Complained of soreness of tongue for 6 months. Motions not foul and frothy. No amœbæ, cellular exudate or fat globule found on microscopic examination, and culture of the faeces was negative. Fat analysis gave total fat 12 per cent. Histamine-fast achlorhydria present. Tongue glazed, red and smooth in the centre. R.B.Cs. 2.4 million. Hb. 32 per cent. On 24th September, 1943, patient was still passing 9 loose motions daily. On 25th September, 1943, she was given 75 mg. nicotinic acid intramuscularly, and the injection was continued daily until 2nd October, 1943. After 3 days of treatment, the number of motions was reduced to 4, and on 1st October, 1943, the patient had one formed motion, the first normal motion in 6 months. She was given 300 mg. nicotinic acid by mouth for 3 more days. Treatment was stopped on 6th October, 1943, and the patient was discharged on 8th October, 1943. Until 29th September, 1943, she was given the fluid diet of the hospital consisting mainly of arrowroot gruel and barley water. Thereafter until 2nd October, 1943, she was given bread in addition, and from 2nd October, 1943, until the date of discharge, she received the full diet of the hospital, e.g. rice sambar (vegetable soup with dhal) and butter-milk. The achlorhydria persisted after treatment.

On 24th November, 1943, the patient returned to hospital with recrudescence of diarrhoea. She was passing 4 or 5 loose motions a day. She was given 50 mg. nicotinic acid intramuscularly for 6 days and was discharged with the diarrhoea controlled.

2. Patient D., female, 65 years. Admitted on 22nd December, 1943, with a history of passing loose motions without blood or mucus 10 to 12 times in the day. No tenesmus, abdominal pain or griping. Soreness of the tongue for 2 months, that is, since the diarrhoea started. Œdema for one month involving the feet, ankles and legs. No amœbæ, cellular exudate or fat globule in the stools, which were not foul or frothy. The total fat in the motion was 9 per cent. Achlorhydria was present. R.B.Cs. 2.1 million; Hb. 30 per cent. On 26th December, 1943, the patient was given 75 mg. nicotinic acid intramuscularly and the injection was repeated daily until 2nd January, 1944. The patient was on the fluid diet referred to above (case 1) until 29th December, 1943. Thereafter bread and boiled eggs were added, and from 1st January, 1944, the patient received the full hospital diet. The number of motions was reduced to 3 by the 28th, and from the 1st the patient began having one formed motion daily. Achlorhydria persisted. The Œdema became worse during the early stages of treatment and involved the thighs. Berin (25 mg. of thiamin intramuscularly) was tried for 4 days without producing increased diuresis or subsidence of Œdema. The patient was discharged on 18th January, 1944, with the diarrhoea controlled and the Œdema considerably reduced. The soreness of the tongue also diminished, but the tongue, though appearing less red and raw, continued to present a smooth glazed appearance.

The patient returned on 5th April, 1944, with a history of passing 4 to 6 loose motions a day. She was given 75 mg. nicotinic acid intramuscularly for 6 days, and the diarrhoea again disappeared.

3. Patient D., female, 45 years. Complained of diarrhoea of 6 months' duration with about 6 motions a day. No amœbæ, cellular exudate or fat globules in faeces. Total fat 6 per cent. Complained of soreness of tongue for 6 months. Tongue red, smooth and atrophic. Œdema of lower extremities for 2 months. Achlorhydria present. R.B.Cs. 2.4 million; Hb. 36 per

cent. Given 300 mg. nicotinic acid by mouth for 4 days. No improvement occurred. Thereafter 100 mg. were given intramuscularly for 4 days, at the end of which the number of motions was reduced to 2 and the motions were becoming formed. The administration of 300 mg. nicotinic acid by mouth was continued for 5 more days. The diarrhoea disappeared. The achlorhydria and the Œdema persisted.

4. Patient M., female, 15 years. Living on monthly family income of Rs. 15 per mensem. Admitted on 7th December, 1943, with diarrhoea of 2 months' duration. History of delivery 3 months previously. Tongue red, papillæ prominent. Motions not foul or frothy. No amœbæ or fat. Culture negative for pathogenic organisms. Hypochlorhydria present. On 8th December, 1943, the patient was given 75 mg. nicotinic acid intramuscularly and the injection was continued daily until 16th December, 1943, by which time the patient was having one formed motion a day. The tongue was less sore and the patient was able to take the full hospital diet. She was discharged on 21st December, 1943, with the diarrhoea completely controlled.

5. Patient D., male, 38 years. Admitted on 21st January, 1944, with diarrhoea of 3 months' duration. Passing about 15 motions a day without blood or mucus. Tongue red and smooth, the papillæ being ironed out. Motions not foul or frothy. No amœbæ, fat or cellular exudate. Total fat 8 per cent. Culture was negative for pathogenic organisms. Achlorhydria present, but histamine injection caused the appearance of free hydrochloric acid in the $\frac{1}{2}$ -hour specimen. Given 75 mg. nicotinic acid intramuscularly on 24th January, 1944. The injections were continued daily until 30th January, 1944, by which the patient was passing one formed motion a day. Achlorhydria persisted after treatment.

6. Patient L., female, 12 years. Admitted on 14th October, 1943, with a history of diarrhoea of over 6 months' duration. Passing about 15 motions a day. Tongue red and smooth. Motions not foul or frothy. No amœbæ or fat on microscopic examination. Hypochlorhydria present. Œdema of lower extremities for 3 months. Complained also of night-blindness. Had 'muddy' conjunctivæ. On 15th October, 1943, 75 mg. nicotinic acid were given intramuscularly and the injection was continued until 22nd October, 1943, by which the patient was passing one formed motion a day. No immediate improvement of the Œdema was observed.

7. Patient D., male, 26 years. Admitted on 4th November, 1943, with a history of diarrhoea of over 8 months' duration. Passing over 15 motions a day. Tongue red and smooth, with fissures. Œdema of the lower extremities present. Motions not foul or frothy. No amœbæ or fat on microscopic examination. Total fat in faeces 6 per cent. Culture of faeces was negative. Histamine-fast achlorhydria present. On 6th November, 1943, the patient was given 100 mg. nicotinic acid intramuscularly and the injection was continued daily until 19th November, 1943. After some initial improvement the diarrhoea persisted and patient was removed home in a moribund state. Nicotinic acid failed to stop the diarrhoea in this advanced and chronic case.

8. Patient C., female, 36 years. Admitted on 25th November, 1943, with a history of diarrhoea of over 6 months' duration. The patient was grossly emaciated. Tongue was red and atrophic and the feet, legs and thighs were cedematous. Achlorhydria present. Motions not foul and frothy. Contained no amœbæ, fat globules or cellular exudate, and culture was negative. The patient was given 100 mg. nicotinic acid intramuscularly on 26th November, 1943, and this was continued until 4th December, 1943. The patient's general condition deteriorated steadily, the diarrhoea persisted and she died on 4th December, 1943.

Discussion

The salient points about the condition described in this paper include the following: it occurs in the poorest section of the community living on grossly deficient diets; it is associated with glossitis which occurs either simultaneously

with the diarrhoea or precedes the onset of the latter; patients are usually in a state of severe malnutrition or even emaciation, œdema being present in a high proportion of cases; the administration of nicotinic acid produces immediate improvement. All these facts suggest that it is a food deficiency disease, presumably related to insufficient intake of nicotinic acid. We have at present, however, no knowledge of how nicotinic acid deficiency actually produces diarrhoea or of how nicotinic acid exerts its curative effect. One of the constant features of the condition is achlorhydria or hypochlorhydria. It has been suggested (Sydenstricker, 1941) that chronic lack of nicotinic acid may lead to reduction of gastric acidity, and, further, that impaired gastric acidity may interfere with the absorption of nicotinic acid. In this way a vicious circle could be created. It is clear, however, that the diarrhoea is not due to loss of the 'acid barrier' of the stomach leading to intestinal irritability, since the achlorhydria or hypochlorhydria persisted after the diarrhoea had been controlled by the injection of nicotinic acid. Moreover, administration of hydrochloric acid, a form of treatment sometimes adopted in cases of this nature, is not of much value.

The condition of the tongue may be an index of changes throughout the intestinal canal, leading to failure of absorption and to intestinal irritability. Clearly, however, atrophy of the mucous membrane of the intestines could not disappear in a few days on treatment with nicotinic acid. The rapid amelioration of the diarrhoea suggests some functional disturbance of the nervous mechanism controlling intestinal peristalsis. This may be associated with changes in the intestinal wall.

The disease differs strikingly from sprue, of which 5 cases were encountered in the course of the investigation. The motions were not the foul, frothy motions characteristic of sprue; no fat globules were found on microscopic examination and the fat content was found to be within the lower limits of normal. The associated anæmia was of the microcytic hypochromic type. The total fat content of the faeces of the sprue cases referred to was over 45 per cent. Contrary to the findings of Manson-Bahr (1941), nicotinic acid given alone was relatively ineffective in the cases of sprue. It appeared to reduce the number of motions, but their essential character remained unaltered and the patients continued to lose weight. It was also noted that a combination of nicotinic acid and riboflavin did not yield better results than nicotinic acid alone in the sprue cases. On the other hand, good results were obtained with injections of crude liver extract. It was found necessary to give much more massive doses of liver extract than the doses recommended for pernicious anæmia. In one of the sprue cases, in which good results were later obtained with crude liver extract, the patient was still losing weight and passing characteristic sprue-like stools after

treatment with nicotinic acid and riboflavin for 36 days during which 3,100 mg. of nicotinic acid were injected by the intramuscular route, 1,800 mg. of nicotinic acid given by the mouth and 36 mg. of riboflavin given intramuscularly. The observation that the dose of crude liver extract needed is greater than that required in pernicious anæmia is in accordance with the experience of Rhoades and Miller (1934). In one of the sprue cases which had relapsed, after what now appears to be inadequate treatment, 4 c.cm. of liver extract daily for a fortnight, and 4 c.cm. twice a week for 4 weeks thereafter, were found necessary to control the disease.

The relation of 'nutritional diarrhoea' to pellagra is a question of considerable interest. Only one of the classic signs of pellagra—dermatitis, diarrhoea and dementia—was present in the condition described in this paper. The word pellagra implies a characteristic skin lesion. Thirty-nine of our cases showed no skin changes, and the crazy pavement dermatosis present in 15 was quite unlike pellagrous dermatitis, and did not respond to nicotinic acid. There was no evidence of mental disturbance. It might be argued that nutritional diarrhoea is in fact early pellagra, and that the signs and symptoms characteristic of pellagra might appear in cases of long duration. But, against this, several of the patients had been suffering from diarrhoea for over 6 months before admission to hospital and in the state of advanced emaciation in which they presented themselves could scarcely be called early cases. The problem of the rarity of classical pellagra among rice-eaters in India has been discussed by Aykroyd and Swaminathan (1940). They pointed out that poor rice diets are often as deficient in nicotinic acid as diets based on maize products associated with classical pellagra.

The present investigation shows that nicotinic acid deficiency does occur in rice-eaters, and is indeed a common and serious condition. Why the clinical picture associated with nicotinic acid deficiency in rice-eaters differs from classical pellagra is a problem for further investigation.

Reference has been made earlier to the severe diarrhoea common in emaciated victims of famine. So-called famine diarrhoea is not a single clinical entity; a number of causative factors are involved. Its relation to the condition described in this paper is not clear, but it is not unreasonable to suppose that nicotinic acid deficiency plays a part in producing the intestinal fluxes associated with famine. Some of the patients in the present series showed a considerable degree of emaciation and resembled in appearance famine victims.

The discovery of a pathogenic agent in cases of chronic diarrhoea associated with malnutrition does not exclude the possibility of co-existent nicotinic acid deficiency. This again is a problem for further investigation.

Finally, it may be remarked that 'nutritional diarrhoea' is not a very satisfactory name for

the condition of which a preliminary account is given in this paper, since the term 'nutritional' is vague. We have not, however, been able to think of a better name.

Summary

1. A group of 54 cases of chronic, non-infective, non-fatty diarrhoea was investigated in the Government Stanley Hospital, Madras. The condition, to which the name 'nutritional diarrhoea', has been given, is associated with emaciation, glossitis, hypochlorhydria or achlorhydria and microcytic anaemia, and seems to be a definite clinical entity.

2. Nutritional diarrhoea was more commonly found in females than males. All patients belonged to the poorest classes and were living on rice diets deficient in quantity and defective in quality.

3. The intramuscular injection of nicotinic acid produced striking and rapid improvement in most cases. Nicotinic acid by mouth was less effective, but was successfully used in mild cases, and in severe cases after initial improvement had been produced by the intramuscular injection of the vitamin.

4. Patients tended to relapse a few months after leaving hospital and returning to their usual diet.

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FULMINATING OR MALIGNANT CEREBRO-SPINAL FEVER

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SPORADIC cases of a fulminating type of cerebro-spinal fever started occurring in the small town of Shorkot with a population of about 8,000 and its neighbouring villages in the month of February 1943. The illness was so severe and death occurred so early, usually within 12 or 24 hours of the onset, that most intensive treatment was necessary. A mysterious disease was said to have broken out in this locality and the public was greatly alarmed. By the 15th April, 1944, 74 patients were examined and treated by us and about half the number was treated by *hakims* and other unqualified practitioners, with hopeless results. A mild epidemic may be said to have occurred in the locality. Four cases of ordinary cerebro-spinal fever were also seen, and have not been included in this series.

Although epidemics of diseases which resembled cerebro-spinal fever have been described during the last three centuries, a classical description of the disease was given first by Vieusseux of Geneva in 1805. Severe cases were characterized by purpuric eruption.

In India and Burma, only one such epidemic has been reported previously. Maitra and Sen Gupta (1940) quoting from the Report on the State of Public Health in Burma for 1937 report the possible occurrence of an epidemic of fulminating cerebro-spinal fever in four village tracts in Haka subdivision, Chin Hill, Burma, in 1937. In this epidemic, there were 103 deaths in three months and a half, but no record of the true nature of this disease is available.

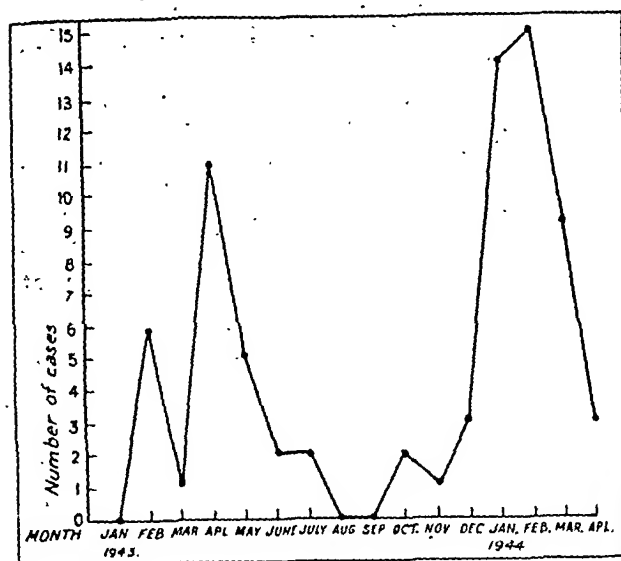
Epidemiological observations

1. *Season*.—The seasonal incidence for 1943 showed that the maximum number of cases occurred in the month of April, when the locality is quite hot. Cases were also met with in the months of June and July which are very hot and dry. The disease seemed to die out in the following three months, again flaring up in the later part of winter.

The graph below shows the seasonal incidence.

2. *Overcrowding*.—Out of 74 cases, 42 came from villages and widely separated huts in the fields and open places. Glover (1918) during the last war showed that an adequate space of more than 2½ feet between the beds reduced the morbidity of the cerebro-spinal fever case to a minimum. In our series, overcrowding does not appear to have been of any importance. The locality being in one of the hottest districts of

the Punjab, most of the people slept in the open, especially during the month of April.



Half of the cases reported from the town actually came from outskirts where there could not be any overcrowding at all.

3. Age.—In the epidemic at Shorkot, the youngest patient was a child of three, and the oldest was a man of sixty-five. No case occurred amongst infants. The maximum number of cases occurred in the age group of 21 to 30 years.

The following table shows the age incidence of this epidemic in detail:—

Age	Number of cases	Age	Number of cases
1-5	4	21-30	22
6-10	6	31-40	7
11-15	16	41-50	4
16-20	13	Over 50	2

4. Sex.—More common in men than in women, in the proportion of 5 : 2.

5. Individual susceptibility.—The spread of the disease is by droplet infection, but why a particular person gets the disease although he may be living under ideal hygienic conditions, is not understood. Usually a second case does not occur in the same house. But we know of a family in a small village where three persons treated by *hakims* died in quick succession, and the fourth recovered with chemotherapy. In our series, in one family, a second case occurred after six months, and the brother of another patient was said to have died of this disease three months earlier. We suggest the possibility of individual susceptibility in this connection.

Laboratory findings

The locality being highly malarial, cases of cerebral malaria occur quite frequently, all the

year round. The cases of cerebro-spinal fever could easily be mistaken for cerebral malaria on clinical examination alone. In the first case brought to our notice, the blood examination did not show any malarial parasite, but revealed neutrophilia. A lumbar puncture and examination of the cerebro-spinal fluid revealed the true nature of the disease.

The fulminating type is essentially a septicæmic condition to start with, involving the leptomeninges secondarily. We could not do blood culture. In one case, the patient had a temperature of 106.5°F. but the cerebro-spinal fluid was not turbid and showed no pus cells or micro-organisms on the first day. There was well-marked polymorphonuclear leucocytosis. On the second day the fluid became turbid with pus cells and meningococci. We could not confirm the view that meningococci of low virulence are readily taken up by phagocytes, and that these cases in which the organisms were mostly intra-cellular were mild ones and vice versa; nor was there any relation between turbidity or the number of micro-organisms seen in the fluid and the severity of the disease. Some cases which proved fatal showed the cerebro-spinal fluid only a little hazy with a few micro-organisms; on the other hand in one patient who died two hours after lumbar puncture, the fluid was full of micro-organisms mostly extra-cellular. As a rule, intra-cellular micro-organisms were not abundant, and they could also be seen lying singly. In three cases the fluid was yellowish but without any red cells.

The cerebro-spinal fluid becomes very thick and slimy in cases of pneumococcal meningitis, but in cases of cerebro-spinal fever, the fluid remains usually thin enough to be readily drawn out through a lumbar puncture needle.

In one case, however, which ended fatally in spite of treatment, the fluid had become so thick and slimy that it could not be drained at all. The smear examination did not show any pneumococci but revealed the presence of meningococci. A similar case has been communicated to us by Dr. Ajmal of Infectious Diseases Hospital, Lahore.

Blood.—All the cases showed marked polymorphonuclear leucocytosis to start with. Average total count was about 15,000 and polymorphs about 85 per cent. No blood film showed any diplococci.

A complement fixation test with sera of patients as advocated by Cruickshank (1941) is said to be a useful test in doubtful cases. This test could not be carried out due to lack of equipment in an out-of-the-way place where the epidemic occurred.

Clinical features

In our series, there was no single sign or symptom on which one could base a diagnosis. The only definite way to establish it was to do a lumbar puncture and examine the fluid.

A typical case.—R. R., 25, H. M. (case 9) was quite well till 11 p.m. on 8th April, 1943, when he went to bed. At 4 a.m. on 9th April, 1943, he woke up, being seized with sudden high temperature and rigor. He vomited twice and at 5 a.m. started complaining of headache. He became comatose rapidly at noon.

Examined at 4 p.m. the same day he had no rash, no stiffness of the neck, reflexes absent, pupils dilated, cornea insensitive, pulse 130 weak, respiration 26, temperature 103.2°F. in axilla.

The patient recovered consciousness slightly, 12 hours after starting the treatment, and was able to take the drug by mouth after 24 hours.

It will be of interest to note that in one case of our series (case 32) the trouble started with pain in the right index finger, spreading from there to the right shoulder and then all over the body, with severe headache. He became completely unconscious within 11 hours of the onset of the illness. He could easily flex his neck three hours before becoming comatose.

No case of our series developed purpura or any other skin eruption. The purpuric rash is said to be characteristic of the fulminating type of cerebro-spinal fever (Banks and McCartney, 1943).

The following table shows the signs and symptoms in 74 cases:—

	Cases
1. Sudden high temperature (above 102°F.) ..	48
High temperature without rigor ..	17
Low temperature (below 102°F.) ..	9
2. Headache—	
Severe	3
Slight	53
Absent	17
Not known	1
3. Nausea and vomiting—	
Present	43
Absent	31
4. Stiffness of the neck—	
Marked	3
Slight	46
Absent	25
5. Unconsciousness—	
Coma :	
Within 12 hours	38
Within 24 hours	21
Within 48 hours	4
Resistant stupor :	
Within 12 hours	4
Within 24 hours	5
Within 48 hours	nil
Absence of unconsciousness	2

Stiffness of the neck and nuchal rigidity were usually so slight that one almost missed it. The best way to elicit this in a conscious patient was to ask him to touch his chest with his chin. It was found to be difficult. In 3 cases where stiffness was not present at all, it became marked after lumbar puncture, and in 2 cases it increased after lumbar puncture (although the general condition improved) but disappeared later on.

Kernig's sign was present more or less in all the cases which showed stiffness of the neck, but this too was a very unreliable sign and was present in a slight degree. Stiffness could also be elicited in several cases which did not show

any change in the cerebro-spinal fluid. Of four children, two had convulsions. Reflexes did not show any uniform peculiarity. Several cases had conjunctival redness. With the exception of one, no case developed delirium before becoming comatose.

Treatment.—The first 8 cases of our series were treated with full (Banks' schedule) doses of sulphapyridine and lumbar puncture; there were five deaths. Thereafter antiserum was added with extremely encouraging results. The town being situated far away from a railway station, and with bad road communications, at times no serum was available in the market, depriving six more cases of its benefit.

The following chart shows the mortality rate in our series:—

Number of cases treated	Moribund when first seen	Cases who left treatment	Died	Mortality rate, per cent*
Without serum. 14	1	Nil	10	71.4
With serum. 60	2	4	5	8.9

* Excluding cases who left treatment.

Since the entire course of the disease may not be more than a few hours, the earlier the treatment is started the better are the chances of recovery for the patient. All patients (11 cases) who received treatment before becoming fully comatose recovered. Even in patients who looked moribund, energetic treatment was sometimes able to save the life. Case 16 was almost dying, with no pulse, irregular respiration, dilated pupils with no corneal reflex, but recovered. Energetic and full treatment will also prevent complications and sequelæ. The giving of small doses of drugs in chemotherapy is harmful as it tends to make the organisms drug fast. *Essentials of treatment are lumbar puncture, antisera and sulphapyridine.*

To start with the lumbar puncture was performed and as much fluid as possible was removed till it came out at the rate of about 30 to 40 drops a minute. In children an ordinary intramuscular needle served the purpose. If the fluid was under great tension and more than 40 c.cm. of fluid could be withdrawn, lumbar puncture was repeated within 12 hours, otherwise after 24 hours, and repeated daily till the fluid became absolutely clear and free from pus cells.

Sulphapyridine.—In our series, we gave to a comatose patient 2 grammes of soluble M&B 693 sodium (Dagenan) intravenously in 20 c.cm. of distilled water very slowly and at body temperature and 2 grammes intramuscularly. Thereafter one gramme was either given by vein or

intramuscularly four-hourly day and night for 3 or 4 days on an average till the patient became perfectly conscious and free from most of his complaints. The drug was given by mouth as soon as he was able to take and retain it. Within the first 24 hours, the patient received 9 grammes of the drug and thereafter 6 grammes daily. The dose was then reduced to 6 to 8 tablets a day for another 4 to 5 days.

Dosage in children.—The usual method of calculating the dose has been to give one gramme for every 5 lb. of weight in infants and one gramme per 10 lb. in children and 20 lb. in adults in 24 hours, but half the 24 hours' dose must be given as soon as the case comes under observation. Banks' schedule (1939) which has been adopted by the Ministry of Health in England is as follows :—

Age period in years inclusive.	0-1	2-4	5-9	10-14	15 and over
Daily amount in grammes.	3	4½	6	7½	9

Crushed tablets could also be introduced into the stomach with a stomach-tube or nasal catheter. If required, the drug could also be given in the form of an enema.

Blood examination of the patient was done to start with and on alternate days for agranulocytosis, and the dose reduced if required. Nicotinic acid in the form of pelonin tablets (Glaxo) was administered in 50 mg. doses for 4 to 5 days after the third or fourth day as a matter of routine. The treatment with M&B 693 was continued till all the symptoms subsided, the leucocyte count became normal and the cerebro-spinal fluid became clear and free from pus cells. Usually this required seven to eight days. In some cases as much as 50 grammes of the drug were given without ill effects. None of the patients developed hæmaturia.

Plenty of fluids must be given to avoid ill effects of the drug. Johnstone and Forgacs (1941) have described 5 cases in which there were cerebral symptoms, identical with those of meningitis, produced by heavy doses of sodium sulphapyridine. This should be kept in mind.

Except for vomiting and nausea none of our cases showed intolerance to the drug. Rash due to the drug occurring in the course of treatment should not be confused with recrudescence of the disease.

Antisera.—Polyvalent meningococcal antiserum prepared by the Bengal Immunity Company and Bengal Chemical Works was used. 40 c.cm. on the average was used intrathecally after the first lumbar puncture, the actual quantity depending upon the amount of the fluid withdrawn. Antiserum was injected daily for three or four days; in urgent cases, 10 to 20 c.cm. was given intravenously as well. The serum should be given with due care. It must be given at body temperature and very very

slowly. In one case while the serum was being given on the fourth day, the patient who otherwise was progressing satisfactorily got a convulsive fit and developed complete unconsciousness, from which she recovered after 5 days. She had never had any serum before. We think the serum was given rather quickly as the patient was struggling a lot and not co-operating.

Meningococcal antitoxin was not used.

General treatment.—Cortical extract was not used. Coramine injections and intravenous glucose saline were given when necessary, and were found to be extremely helpful.

None of our cases showed any abscesses after intramuscular injections of the drug.

Complications and their treatment

1. *Delirium.* On the second day of the treatment patients usually recovered consciousness to a large extent, but many cases became very restless and boisterous. It became very difficult to control them for lumbar puncture. Patients were put on barbiturates and bromides. Gardenal in half-grain doses with chloralhydrate and potassium bromide, or paraldehyde was found to be quite effective.

2. *Excruciating pains in back joints and limbs.* They became marked in many cases on the second day or the third day of treatment, and were successfully treated with the usual drugs.

3. *Painful swelling of the joints.* This appeared in 14 cases but subsided within four or five days of general treatment. It did not require any special treatment. Usually the fingers, wrist and elbows were involved, rarely the knee joints.

4. *Vomiting and nausea.* It was also a troublesome complication in a large number of cases. Sodium bicarbonate, hydrocyanic acid, mustard plaster, chloretone, ice, etc., were found to be effective. In intractable cases, intravenous administration of 5 per cent glucose or sodium bicarbonate solution was found to be useful.

5. *Herpes labialis.* It appeared in fifteen cases, and did not require any special treatment.

6. Only one patient developed internal squint of the right eye, but recovered subsequently.

7. One case developed deafness.

No other case developed any complications such as cranial nerve paralysis, abscesses, paralysis of the extremities, pneumonia, conjunctivitis, otitis media, orchitis, hydrocephalus, etc.

None of the cases had a relapse, but it should be kept in mind especially when the dose of the drug has been reduced early.

Discussion

In acute or ordinary types of cerebro-spinal fever there is a stage of irritation followed after a week by a stage of resistant stupor (Price, 1937). In the superacute type, acute delirium is present for the first three or four days, and is followed by stupor and coma. In the fulminating type the disease takes a much more rapid

course. The untreated patient may die within a few hours of the onset of the disease. Cases of intermediate types are undoubtedly met with, and the classification is only arbitrary. We have regarded our cases as of the fulminating type because out of 74 cases 68 developed coma or resistant stupor within 24 hours and four within 48 hours of onset. Two cases in which there was no loss of consciousness were early cases. After having seen a number of cases, we made it a rule to do lumbar puncture in all patients who developed sudden high temperature with rigor, headache and vomiting, and who showed no malarial parasites in the blood. These patients reported to us within a few hours of the onset of disease. Lumbar puncture gave positive results. We are sure that these cases would have developed unconsciousness had we waited for a few hours more. Four cases of ordinary cerebro-spinal fever were also seen, and have not been included in the series.

The fulminating type of case has been described since 1906, under the heading of 'adrenal apoplexy' (Andrewes, 1906), but the number of cases reported is very small. Waterhouse (1911) described another case, but no micro-organisms were isolated by him. In 1916 Maclagan and Cooke mentioned the post-mortem findings in two cases of this type and isolated meningococci. The characteristic findings in these cases were hæmorrhages in the adrenals. In 1918 Friderichsen also described the condition. It is called Waterhouse-Friderichsen syndrome, but in our opinion should be called Waterhouse-Andrewes syndrome, since Andrewes described the condition much earlier. Maclagan and Cooke were the pioneers in suggesting treatment of the condition by adrenal cortical extracts.

Grace *et al.* (1940) and Banks and McCartney (1943) and several others have also described some cases of this type and their treatment. About a hundred cases have been reported so far. Now it is believed that only about 60 per cent of the cases of this syndrome are due to the meningococcus, the rest by other micro-organisms such as the pneumococcus, streptococcus hæmolyticus. So far there is not enough evidence to prove that all cases of the fulminating type of cerebro-spinal fever are necessarily those of 'adrenal apoplexy'.

With the introduction of chemotherapy, and especially with a drug like sulphadiazine, treatment of ordinary cerebro-spinal fever has become quite satisfactory, but the results of treatment of fulminating type have been disappointing. Bryant and Fairman (1939) in the absence of a soluble drug used a suspension of 0.5 grammes of M&B 693 in 10 c.cm. of normal saline intramuscularly in the Sudan. They claim to have treated a consecutive series of 20 cases of fulminating type with a single intramuscular dose of 1.5 grammes and by lumbar puncture. We were not so fortunate. Harries (1940) described a new treatment for acute fulminating cerebro-spinal fever with 5 per cent glucose saline intravenously, synthetical cortical extract, sulphapyridine and antitoxin intramuscularly. He treated several cases successfully (1942). Varma (1941) published 9 cases of cerebro-spinal fever out of which two were of fulminating type, and both proved fatal. He gave them combined treatment but his doses were small and inadequate. Morrison and

Houghton (1943) reported a case of fulminating type with recovery of consciousness three hours after an injection of 2 grammes of sulphapyridine. Grant and Wotzilka (1943) reported another case with recovery of consciousness two hours after an injection of sulphapyridine given intravenously. Lindsay (1943) described another such case.

The value of serum in combination with full dose of sulphanilamides has not been disproved even in ordinary cerebro-spinal fever cases. The statistics collected by Jubb (1943) show that mortality was higher in combined treatment than with chemotherapy alone, but as these figures were collected from more than 60 hospitals, the possibility that the serum was administered to more severely ill patients was not ruled out. Hunter (1940) believes serum to be of value in very severe cases. The observations of Jordan *et al.* (1940) also are in favour of combined therapy.

Summary

Seventy-four cases of acute fulminating type of cerebro-spinal fever have been described, of which fourteen were treated with lumbar puncture and sulphapyridine with a mortality rate of 71.4 per cent (including one moribund case), and 60 cases with triple treatment of serum, lumbar puncture and sulphapyridine with a mortality rate of 8.9 per cent (including two moribund cases). It is safer to depend on all the three methods than on sulphapyridine alone for this type of case. With triple treatment, not only is the mortality rate greatly reduced but also sequelæ are usually absent. Although most of the cases were definitely of the acute fulminating type, none showed any purpuric rash or petechial hæmorrhages which are said to be always present in this condition.

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AMŒBIASIS OF THE ANUS AND PERINEUM

WITH REPORT OF A CASE

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IN 1912 Maxwell read a paper before the Society of Tropical Medicine and Hygiene entitled 'Fistulous Disease of the Buttocks: a clinical entity'. Under this title he described a disease occurring in South Formosa and probably also in South China. The disease was rare. It began, according to the statement of the patients, as an ordinary fistula-in-ano, and from this fistulous tracks spread in all directions over both buttocks; the whole area was riddled with a mass of tracks communicating with each other and marked on the surface by raised and indurated lines. Here and there small pin-hole openings which discharged serous pus were seen; actual pain was slight but there was often marked discomfort on sitting. The disease was not tuberculosis or syphilis. Treatment was unsatisfactory and total excision impossible on account of the extent of the lesion. Since he had started to look at the pus microscopically, Maxwell said:—

'I have found in all of the few cases that have come to hospital the presence, and that in large numbers, of amœbæ, conforming, I believe, to the type of *Entamoeba histolytica*; and I venture to throw out the suggestion for further investigation that the disease is due to the entrance of these amœbæ into the tissues, possibly from an original simple fissure-in-ano.'

In the discussion which followed, Wenyon refused to allow the presence of amœbæ as proof of the pathogenicity of the disease. Since then Maxwell's paper has been more or less forgotten, but proved cases of amœbiasis of the skin of the perineum and buttocks have from time to time been reported, and there are in the literature notes of nineteen such cases. The majority of these have been encountered in China.

That amœbæ are capable of causing ulceration of the skin has been known for some time, but reports of cases have often been unconvincing.

Carini (1912) reported two cases occurring after opening liver abscesses. Ngai and Frazier (1933) were able to collect twenty-seven cases of amœbiasis cutis but after careful consideration they rejected all except four as not carrying sufficient proof of the protozoal origin of the complaint.

Ngai and Frazier classified the cases into three groups:—

1. Seventeen cases exhibiting a progressively gangrenous and ulcerative lesion over the abdominal or thoracic wall following spontaneous rupture or operative incision of some pre-existing intra-abdominal amœbic focus, e.g. liver abscess or ulcerative colitis.

2. The second group consisted of four cases of eczematous dermatitis, three of ulcerative dermatitis of the trunk and extremities without open abdominal foci of infection and one of penile ulceration following 'anal coitus'. All these cases they consider to be of doubtful authenticity.

3. The third group comprises two cases characterized by chronic ulcerative fistulous or condylomatous lesions of the perineal region and buttocks both of which followed chronic dysentery of undetermined ætiology [van Hoof (1926) and Tixier *et al.* (1927)]. Ngai and Frazier reported three further similar cases. It is with this third group of cases that the present paper is concerned.

Hu (1937) was able to collect from the literature nine, and to report nine further similar cases. Unfortunately he was chiefly concerned with the histopathology of the condition and all but one of his cases were unsuspected until diagnosed histologically after operation or biopsy and he gives no clinical details. Table I (modified after Hu) gives the site and type of all the cases reported to date. Hu considers that the condition is probably more common than is at present realized. It appears to be always secondary to some fissure, abrasion or other breach in the continuity of the epithelium. The case at present reported bears this out.

TABLE I

Year	Author	Site and type of lesions	Number of cases	Sex
1926	van Hoof	Perianal buttock ulcers and anal fistulæ.	1	F.
1927	Tixier <i>et al.</i>	Perianal ulcer	1	M.
1932	Lee	Secondary infection of carcinoma of cervix.	2	F.
1933	Ngai and Frazier.	Perianal ulcer	1	M.
1933	Ngai and Frazier.	Ulcer of urethra	1	F.
1933	Ngai and Frazier.	Secondary infection of papilloma of anus.	1	M.
1933	Crawford	Perianal abscess; ulcer buttocks.	1	F.
1931	Engman and Meleney.	Gangrene of buttock, perineum and scrotum.	1	M.

TABLE I—*concl'd.*

Year	Author	Site and type of lesions	Number of cases	Sex
1935	Wu and Chi	Cervix uteri	1	F.
1937	Hu	Papilloma of anal region, ulcerated and bleeding.	1	M.
		Papilloma of anal region.	3	M.
		Ulcerated papillomas of labia majora and minora.	1	F.
		Abscesses, ulcers, sinuses and fistulae around anus.	1	M.
		Nodule in perineum, later ulcerated.	1	F.
		Endocervicitis	2	F.
		TOTAL ..	19	
		Youngest—17 years		
		Oldest—61 years		

Case report

Mrs. S., an Anglo-Burmese lady, was admitted to a hospital on 4th September, 1942. She was 35, and had one child aged two. She complained of 'piles' which she said she had had for many years. Ten years previously she had had amœbic dysentery and two years ago malaria.

History.—At the beginning of January 1942 air raids forced her to leave her home in Rangoon. For the next few months she spent her time moving on account of enemy action from one temporary dwelling to another. Eventually she found herself at Mogaung and from there started the 180-mile trek to Kohima. Most of this journey was made on foot. Food while in Burma was obtained from the villages along the route. After the Indian border was crossed organized camps provided rations. While crossing the frontier she began to pass blood and mucus. At first, tenesmus was severe and motions were passed every five to ten minutes. Her baby also had blood and mucus in her stools. The complaint lasted fifteen days and then cleared up.

On about 15th June she found that she had a 'blind boil' beside her piles. This became so painful that she could not walk, and had to employ coolies to carry her in a litter.

On her arrival in Calcutta, about one month before admission, she was treated in hospital for malaria but left on her own responsibility after two days. About one week before leaving Calcutta she noticed a discharge from her rectum and applied 'Rexol' with great relief. Two days later she noticed a vaginal discharge. During the four days' train journey to the station whence she was admitted, the condition became rapidly worse.

On admission, she was found to have a fungating mass about the size of a large walnut around the anal orifice which was yellow and pink in colour and exuded pus from the whole surface. From this mass an ulcer with considerable œdema around the edges, which were undermined, spread forward over the perineum and into the posterior wall of the vagina. On separating the labia majora large quantities of pus exuded. The whole area was intensely tender, and a vaginal examination was impossible.

She was toxic, and her temperature was between 101°F. to 102°F. There were no abnormal physical signs in the circulatory or alimentary system.

A sample of serous exudate taken from the edge and floor of the ulcer by the capillary tube revealed abundant trophic amœbæ which contained red blood cells and exhibited the typical mobility and pseudopodial characteristics of *Entamoeba histolytica*.

Blood films revealed ring forms of *Plasmodium falciparum*.

Treatment.—Six daily doses of emetine gr. 1 were given at night. The ulcerative area was treated with hot saline washes and fomentations followed by painting with mercurochrome. The bowels, which were costive, were kept open with Agarol and liquid paraffin. The malaria was treated along the usual lines.

Progress.—Definite improvement was noticed twenty-four hours after the first injection. After the third the affected parts were tender, but very little pus or blood was present. After the fifth there was no discharge from the vagina although the area around the anus was very tender. It was now definitely seen that the mass around the anus was hæmorrhoidal.

The patient was discharged on the eighteenth day free from all symptoms except those referable to the hæmorrhoid. At no time while in hospital did she have any signs of dysentery.

Discussion.—According to Hu 'amœbic infection of the genito-anal region varies a great deal in its gross appearance. In some cases it manifests itself merely as minute ulcers of the already existing papillomas, fistulae, etc. In others it may be in the form of extensive ulceration or even gangrene'. In the first group diagnosis is difficult and, as in all but one of Hu's cases, only made on careful histological examination. In the second group the appearance may be alarming as they were in the case reported above. Diagnosis has to be made from ulcerative granuloma of the pudenda (granuloma venereum), condylomata and tuberculous condition. A previous history of dysentery may help, but dysentery is so common in the East, that little reliance can be placed on this, and cases have been reported showing no previous history of dysentery (Wu and Chi, 1935).

Amœbiasis cutis has been noted to be an extremely painful condition (Engman and Meleney, 1931; Crawford, 1933; Ngai and Frazier, 1933). The pain in this case was severe, and on any attempt to handle the lesion the pain became excruciating. Pain is not a prevailing feature in the granulomas.

Nearly all the reported cases have arisen secondarily to a previously present lesion of the skin; fissures-in-ano, papillomas, condylomata and carcinomatous conditions are reported. A much abraded hæmorrhoid was the first nidus of infection in this case, and it was the combination of a history of dysentery during a period of extreme hardship involving a great deal of walking and the reported presence of the hæmorrhoid which first aroused a suspicion of the nature of the case. The colour of the lesion—a mixture of pinks and yellows reminiscent of the amœbic colon—also helped in making a decision.

Tixier *et al.* (1927) drew attention to the presence in their case of colonies of amœbæ deep down in the dermis away from the surface ulceration. Hu (1937) confirmed this. It is suggested that a positive diagnosis can more easily be arrived at by withdrawing serum from deep in the tissues around the ulcer margins, as in searching for *Leishmania tropica* in oriental sore and spirochætes in a primary sore. In the case under review, the serum so withdrawn contained a suspension of amœbæ practically free from pus and red cell.

No case of amœbiasis cutis of the perineum has been previously reported from British India or Burma nor has any account of such cases been reported in British medical literature. The disease, however, appears to have occurred wherever amœbiasis is particularly common. It is felt that the rise in the incidence of amœbiasis which has been noticed in recent years in India may be accompanied by an increase in its local manifestations. There is a grave risk that such cases may be diagnosed by the unwary as venereal in origin.

Summary

1. The literature concerning nineteen cases of amœbiasis cutis of the anal and perineal region is reviewed.
2. Such cases fall into two groups :—
(a) Those exhibiting small ulcers only, secondary to previous papillomas, fistulæ, etc.
(b) Those showing extensive ulceration and tissue destruction.
3. A case of the latter type is reported.

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SOME PHYSICAL AND IMMUNOLOGICAL REACTIONS OF RBC 'JUICE' AND STROMA

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THE following experiments with rbc juice and stroma were undertaken to answer two questions : 1. Is the Hb in solution inert with an anti-serum-protein serum and a blood-group specific Rh serum, and anti-M&N serum (such as anti-debris instead of whole cells which may not be compatible with the blood of the animal injected ? The first question is of medico-legal importance and the second of considerable immunological interest. The answer to both the questions was in the affirmative.

The coloured rbc juice

Reaction with ordinary anti-sera (anti-serum-protein sera).—Human rbc were washed in three changes of saline. The saline from the last washing did not react with the anti-human serum. The packed deposit was hæmolyzed with nine volumes of distilled water, the contact lasting over twelve hours at ice box temperature (short of freezing in a refrigerator). The transparent coloured fluid was passed through Seitz filter. It frothed, on shaking, like coloured serum. It was diluted with normal saline (about 50 fold) until its froth equalled that of a known (possibly more, not less). It did not give a ring with the standard anti-human serum (Sutherland, 1907, 1910; Dean, 1931; Lloyd, 1935). Sheep and monkey rbc similarly treated also gave negative reactions with their respective anti-sera.

Reaction with blood-group specific serum.—The 1 in 10 suspensions in water of the water-damaged human rbc showed distinct clumping on the slide with equal volumes of the homologous sera (containing the appropriate isonin—iso-hæmagglutinin) before filtration but none after filtration. This is in accordance with the observation ascribing the clumping to the stroma present (Wiener, 1939) in the fluid which was believed to be a lysate (Dold and Rosenberger; Ottensooser and Zurukzogu, quoted by Wiener). The conclusions emerge that the specificity of the serum protein and that of the isogen (iso-hæmagglutinin) do not go beyond the stroma of the rbc.

The specificity of the hæmoglobin.—This has been established (Hektoen and Schulhof, 1922 and 1923.) It has even been suggested that the test for blood for forensic purposes should

be based on the specificity of the hæmoglobin rather than on (i) the presence of blood established by physico-chemical means and (ii) the specificity of the serum protein established by immunological means. The barrier of the stroma between this Hb specificity which does not pass into the serum and the serum specificity which does not pass into the Hb, however, has not been definitely acknowledged and stated.

Further specificities appear to have been confused in the matter of the mechanisms of the production of hæmolysis: . . . 'the portion of the erythrocyte that is responsible for the production of hæmolysin is a moot question. Bordet and von Dungern maintain that the stroma is the exciting agent; Nolf and others believe that the stromata produce hæmagglutinins, and that the hæmoglobin is chiefly concerned in the production of hæmolysin' (Kolmer, 1923).

Certain saline extracts of blood stains tested for medico-legal purposes present an apparently incongruous combination of good froth and colour and poor or negative reaction with the anti-sera usually employed. They can be prepared experimentally from clots which have been drained of serum and dried. The explanation is that in them there is a sufficiency of the colloid hæmoglobin (hence the colour and froth) but paucity of the serum protein (due to drainage). Such extracts could be tested by hæmoglobin specific anti-serum after excluding the 'possible overlapping of the reaction in related species' (Hektoen and Schulhof, *loc. cit.*).

The stroma

Restoration of opacity in laked rbc.—On replacing the water of the transparent stroma suspension by normal saline (by transferring the watery suspension to a test tube in which an equivalent quantity of normal saline has been evaporated to a dry residue) a remarkable change comes over the stroma. The suspension turns opaque almost like the normal rbc suspension in saline. On centrifuging a coloured deposit falls to the bottom of the tube under a column of deep red and transparent fluid.

Microscopic appearance of the water-damaged rbc.—The rbc in the deposit are damaged. Microscopically, some are distended but unsubstantial; others are shrunken. The yellow colour appears to be confined to a peripheral zone of small vesicles. Biconcavity appears to be retained on the whole. Under the dark-ground illumination the peripheral zone presents a honeycombed appearance. Staining is poor. This is not the final description of the water-damaged rbc.

Preparation of anti-Rh sera from stroma.—Strong agglutinating sera against the rbc of *Macacus rhesus* have been obtained by injecting fowls intravenously with the stromata of the rbc in saline. One such serum in a 1 in 1,000 dilution in saline has agglutinated the fresh rbc in one hour (the time allowed for work on Rh antigen).

The strong agglutinating sera exerted two other actions: (i) they hæmolysed the rbc in the presence of the complement and (ii) produced a precipitate with a weak dilution (of the order of 1 in 1,000) of monkey's serum. These actions were not strong. The hæmolytic action of the fresh unheated and undiluted serum was not so brisk as that of the anti-serum produced against entire rbc in rabbits. The ring of the precipitate did not appear for over 5 minutes (instead of under 2 minutes as with an anti-serum prepared from serum). The stroma, therefore, was strongly agglutinogenic but moderately lysogenic and precipitogenic.

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EXPERIMENTAL STUDIES IN RAT-BITE FEVER*

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and

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SINCE the publication of a detailed report on rat-bite fever in Calcutta by Chopra, Basu and Sen (1939), further work on the subject was analysed and the results put in this note. The present paper reports the course of the disease in laboratory animals, namely, guinea-pigs, white rats, white mice and kittens. This study is of special importance in connection with diagnosis of the disease by animal inoculation as well as chemotherapy of the disease. The negative phases in the animals must not be mistaken for

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failure to infect. In table I the course of the disease in various animals is shown:—

attack varied from 1 to 34 days; the average being 12.1 days. Up to 3 relapses have been

TABLE I

Showing the course of the disease in guinea-pigs, white mice and white rats

	GUINEA-PIGS		WHITE MICE		' WHITE RATS	
	Range, days	Average, days	Range, days	Average, days	Range, days	Average, days
Incubation period ..	3-23	10.2 in 39	4-6	5.2 in 10	3-17	8.3 in 10
Period of initial attack ..	1-49	10.3 in 39	1-34	12.1 in 10	1-6	3.1 in 10
1st negative phase ..	2-38	7.2 in 31	1-5	2 in 6	1-6	2.8 in 9
1st relapse ..	1-37	12.5 in 26	4-16	9.6 in 5	1-5	2.7 in 9
2nd negative phase ..	1-9	4.8 in 17	2-3	2.3 in 3	1-75	14.5 in 7
2nd relapse ..	1-36	10.2 in 14	3-6	4.6 in 3	1-10	5.6 in 6
3rd negative phase ..	1-26	7.9 in 8	3	3 in 1	6-142	34.3 in 6
3rd relapse ..	4-17	5.8 in 4	2	2 in 1	5-8	6.5 in 2
4th negative phase	12	12 in 2
4th relapse	25	25 in 1
5th negative phase	10	10 in 1
5th relapse	4	4 in 1
6th negative phase	5	5 in 1
6th relapse	2	2 in 1
7th negative phase	34	34 in 1
Survival ..	6-101	37.2 in 44	2-120	34 in 12	9-170	63.1 in 13

0.25 c.cm. infected blood was inoculated intraperitoneally into 44 guinea-pigs. *S. minus* did not appear in the blood of 5 guinea-pigs which died between 6 and 15 days after inoculation. The remaining 39 became infected. The incubation period varied from 3 to 23 days, the average being 10.2 days. The period of initial attack (i.e. when *S. minus* first appeared in the blood) varied from 1 to 49 days, the average in 39 being 10.3 days. Up to 3 relapses have been observed in the guinea-pigs. The disease does not seem to be a febrile one in the guinea-pigs. The temperature varied from 100°F. to 106°F. during the incubation period, during periods when there was *S. minus* present in the blood as well as in the negative phase. After the spirillum appears in the blood the animals lose in weight. These 44 guinea-pigs lived from 6 to 101 days, the average being 37.2 days. During the height of infection, 2 guinea-pigs were killed and their internal viscera were examined under dark-ground illumination. The brain, kidney, lungs, liver, spleen, bone-marrow, submaxillary and sublingual glands showed very scanty infection, and clean guinea-pigs inoculated with emulsions of the above tissues became infected, but the incubation period was invariably prolonged (20 days or more). (Two infected gravid females gave birth to young ones whose blood was found negative, and the young ones were found susceptible to infection with the organisms.)

White mice.—Twelve white mice were inoculated intraperitoneally with a few drops of infected blood. Two died 2 to 3 days after inoculation. The rest took the infection. The incubation period varied from 4 to 6 days; the average being 5.2 days. The period of initial

observed in the mouse. The infected mouse has been observed to live as long as 120 days, the average as observed in 12 inoculated mice, being 34 days.

White rats.—Thirteen white rats were inoculated intraperitoneally with a few drops of infected blood. Ten took the infection. The incubation period varied from 3 to 17 days, the average being 8.3 days. The initial attack lasted from 1 to 6 days, the average being 3.1 days. Up to 6 relapses have been observed in white rats. The infected rats were found to live from 9 to 170 days, the average period being 63.1 days. Three of the white rats were found refractory to repeated inoculations. They died on the 44th, 59th and 95th days respectively after first inoculation.

Kitten.—One kitten was inoculated intraperitoneally with $\frac{1}{2}$ c.cm. infected blood. It became infected on the 11th day, its blood remained positive for the subsequent 10 days, after which it died.

Another kitten was made to ingest 2 c.cm. of infected blood. This kitten was not infected though it lived for 23 days after ingestion.

Cats prey on rats. It may be that in nature, infection passes from rat to cat and *vice versa*.

Culex fatigans.—One hundred and sixty-six *Culex fatigans* were fed on infected (++) white mice. The guts, salivary glands and the coelomic fluid of the survivals were examined under dark-ground illumination, and it was found that *S. minus* will not survive in the mosquito's gut even for 24 hours. The salivary gland and coelomic fluid were always negative.

Rat-flea.—Two hundred and thirteen rat-fleas were fed on infected (++) white mice, and the survivals were dissected at different intervals

of time and were examined under dark-ground illumination for *S. minus*. Up to 24 hours, motile *S. minus* were found in the gut. Salivary glands and coelomic fluid were always negative.

Summary

The course of the disease in guinea-pigs, white mice and white rats has been studied. After incubation periods varying for the three different animals, *S. minus* appears and disappears several times. Three relapses have been seen in guinea-pigs and white mice and as many as 6 relapses have been seen in white rats. The disease does not seem to be a febrile one in guinea-pigs. From the period of life it can be said that it does not inconvenience the rats.

The disease does not seem to be transmitted by *Culex fatigans* and rat-fleas.

Acknowledgment

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AMOEBIASIS AND BLACKWATER FEVER

By CHRISTIE MCGUIRE, D.T.M.

BLACKWATER fever has been reported in the Bengal Dooars for over 50 years. The district is situated at the foot of the Bhutan hills and is continuous with the Terai belt of forest. It is the chief tea-producing area of Bengal, and there are numerous tea-gardens where malaria is hyperendemic. The average spleen rate was about 65 per cent before anti-malaria measures were undertaken. In one area it was over 90 per cent, but since the introduction of these measures the spleen rate has been much reduced with a fall in the incidence of malaria and blackwater fever. Due to the war, difficulty in obtaining oil for spraying is being experienced, and the spleen rate is rising.

During the past 12 years, I have seen 33 cases of blackwater fever in my practice in the Dooars. The history of these cases was always the same, namely, repeated attacks of malaria which were controlled by quinine, then suddenly blackwater fever developed during one of these attacks after taking quinine. Cases of blackwater fever occurring without quinine have been reported from elsewhere, but this was not my experience.

A popular view about the aetiology of blackwater fever among the medical practitioners in the Dooars is that it has something to do with the liver. This is interesting in view of the recent important work of Krishnan and Pai (1936) and my clinical observations.

Krishnan and Pai (1938) after studying the biochemical blood changes in blackwater fever conclude that liver damage and altered metabolism are factors in the aetiology of the disease. My clinical observations show that amoebic hepatitis is present in a large percentage of these cases. I shall deal with the latter first.

What struck me forcibly in the 33 cases of blackwater fever that I saw was the large number suffering from amoebiasis with secondary hepatitis. In 21 of these cases (63.6 per cent), the clinical signs of amoebiasis, viz, tender and thickened caecum and ascending colon, and enlarged and tender liver were present and microscopical examinations of their stools showed *Entamoeba histolytica*. In 9 cases, though the clinical signs of amoebiasis were present, no protozoa were found in their stools. One patient left the district before full investigation, and 2 patients died.

Regarding these 9 cases, it is being increasingly recognized that sigmoidoscopic examinations are sometimes positive when microscopical examinations are negative. In this series, only microscopical examinations were done. Further, the cases that were microscopically negative were examined again a month after their blackwater fever subsided, the clinical signs still being present, they were given emetine and the symptoms subsided.

The presence of amoebic hepatitis noted in these cases of blackwater fever may help to explain the liver damage and the associated biochemical blood changes which Krishnan and Pai have reported. They estimated the blood cholesterol not only as total cholesterol but also as free and ester cholesterol. Previous workers had estimated the blood cholesterol only as total cholesterol with variable and inconclusive results. Krishnan and Pai also found, like other workers, the total cholesterol estimations to give variable and inconclusive results, but when they separated the total cholesterol into free and ester cholesterol they found a rise in ester cholesterol and marked fall in free cholesterol in all cases.

They concluded from these findings that the evidence in favour of damaged liver is overwhelming. In their opinion, the production of the haemolytic agent as well as the conditions that favour its action seem to be the result of altered metabolism due principally to liver injury. Manson-Bahr (1940) discussing the mechanism of haemolysis in blackwater fever says that 'derangement of metabolism is an attractive hypothesis'.

One of the causes of liver damage may be chronic malaria. It is the experience of practitioners in blackwater fever areas that a new arrival in a hyperendemic zone may suffer from the most virulent forms of malaria, viz, cerebral, algid, dysenteric, etc., but not blackwater fever. Some period of residence is required. During that time he will suffer from frequent attacks of malaria before the onset of blackwater fever.

The minimum period of residence that I observed was 2 years, though others have reported less.

Now, besides malaria, the Dooars is notorious for amœbiasis. It is not common in the labour forces of the gardens, but it has a special predilection for a certain class of people such as Europeans, Bengalees, Punjabis, Marwaris, Chinese and up-country Hindus of the dhobi and sweeper class, and strangely it is in these people in whom blackwater fever is most prevalent.

Manson-Bahr writes that some workers recognize a pre-blackwater stage. One of the signs is 'an enlarged and tender liver'. Unfortunately, he does not mention if these workers noted whether or not the 'enlarged and tender liver' was still present after the blackwater stage had passed off and if emetine was required at some future date. Then some conclusion as to the cause of the 'enlarged and tender liver' could have been formed.

It may be that the amœbiasis in my series of blackwater cases is coincidence. This factor must be considered but in view of the work of Krishnan and Pai it is possible that amœbic hepatitis may, in some cases, cause liver damage of a type that will help in the production of the biochemical blood changes reported by them, especially when these cases suffer from a superimposed malarial infection. Quinine may, in these cases, cause further deterioration and act as an immediate excitant.

The exciting cause in all my cases of blackwater fever was quinine, which was taken either orally or by injection. In two cases where it was restarted the blackwater fever recurred and atabrin was substituted. In the other cases, quinine was immediately stopped and either oral or parenteral atabrin given. In no case did blackwater fever recur after atabrin. The usual glucose and alkali treatment was also given, and some received *vitek peduncularis* in addition.

After convalescence, all patients were treated for amœbiasis with emetine and carbarsone. Later, they were advised to take 5 grains of suppressive quinine daily, and in case of any malarial rise in temperature, they were further advised to stop the quinine and take atabrin. There was no second attack of blackwater fever in any case but as they now took atabrin, instead of quinine for any rise in temperature, no opinion can be given.

In the Dooars, there are a number of people, especially Bengalees, who suffer from chronic malaria and amœbic hepatitis, and it would be interesting to know if the blood changes in these people correspond to the changes reported by Krishnan and Pai in blackwater fever.

Conclusion

The importance of liver damage, partly due to amœbiasis, as a predisposing cause of blackwater fever, is stressed.

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ORIENTAL SORE IN THE NIZAM'S DOMINIONS SOME EPIDEMIOLOGICAL FACTORS

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THE occurrence of oriental sore was first reported in H.E.H. the Nizam's Dominions by Young (1937) at Jalna as a condition simulating certain aspects of leprosy. Daver and Ahmed (1943) again reported the incidence of this conditions not only in Jalna but also in Pattan, a town in the Aurangabad district 72 miles from Jalna.

However late the disease may have been reported from these parts, the occurrence is by no means so recent as it seems. Many stories are in vogue in the affected areas regarding its importation, but the most plausible explanation is that it was introduced by the Moghal troops of Aurangzeb's days. The disease was rampant in the Moghal Empire's capital; hence it was called 'Delhi Boil', and it affected the Emperor Aurangzeb after whom it is also known as 'Aurangzeb Phora' at Delhi (Shah, 1941).

With a view to obtaining more definite information regarding this disease and the extent to which it prevailed in the affected parts, the present epidemiological survey was undertaken, and the junior author was specially entrusted with part of the work dealing with the vector (sand-flies). Unconfirmed reports of the occurrence of the disease in Aurangabad town led to the inclusion of the survey of this town during the present enquiry.

Methods employed.—A house-to-house search was made in the localities in the towns surveyed both for cases as well as for sand-flies. Details of the cases with age, sex, period of residence in the locality were recorded. Cases were first diagnosed clinically, but later in the majority of instances, diagnosis was confirmed by the demonstration of leishmania in smears taken from the sores. All sand-flies collected were first classified, and female sand-flies from houses where cases of oriental sore were found were dissected to detect the flagellate infection. Gravid females were specially chosen for dissection, as gravidity ensures that the fly has had at least one blood feed; since it is observed that

the development of the ovary is not possible unless it has taken the first meal of blood (McCombie-Young, Richmond and Brendish, 1926). Moreover, the development of the parasite is much more rapid in gravid females than in the unfertilized flies (Shortt, Barraud and Craighead, 1926). Search was also made for phlebotomus larvæ with a view to studying their bionomics, habits and habitat.

In all the three towns surveyed, schoolboys and girls were specially examined with a view to finding the incidence of the disease among this particular group of the population.

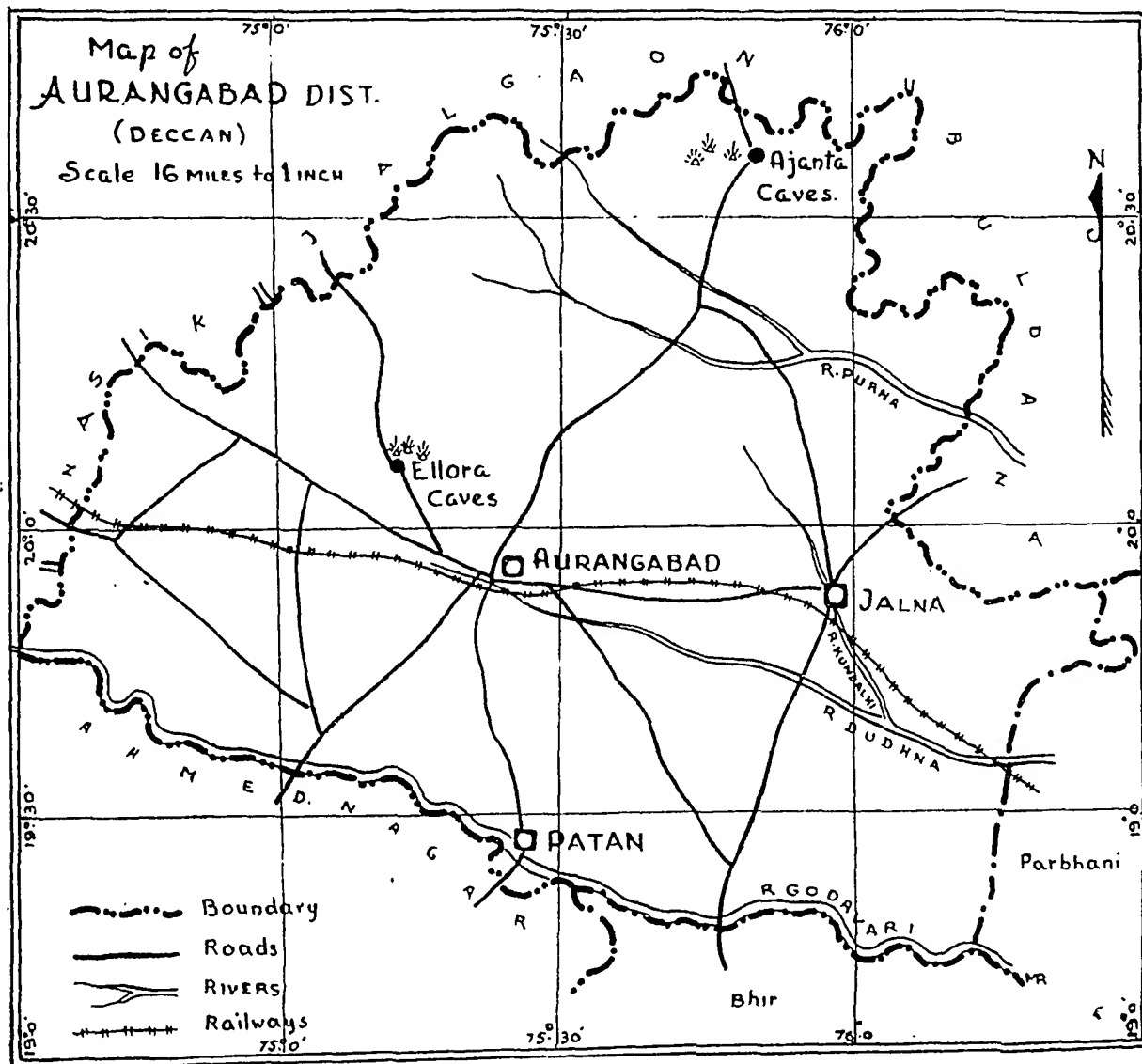
The three towns surveyed are indicated in the map, which shows their disposition in relation to one another and the existing communications.

Aurangabad is the headquarters of the district and the Division (Suba) of the same name.

The population of the town is 50,924. The Kham river, which is a tributary of the Godavari, flows through the town. The city proper is on its eastern bank; the cantonment and a suburb of the city are on its western bank. The mean height above sea level is 1,885 feet and the surface soil is loamy.

Aurangabad was the capital of the Moghal Empire for some time during the reign of Aurangzeb. After the disruption of the Moghal Empire and the shifting of the capital to Hyderabad by the Asif Jahi dynasty, the town lost its fame and importance, and most of it now is but a heap of ruins. The older houses are generally multi-storied ones; the ground floor in most is used as cattle sheds. In poorer quarters even these ground floors, dark and damp, serve as living rooms.

Jalna is the headquarters of the taluq of the same name, with a population of 22,408. It is a commercial centre dealing mostly in cotton and grains and has



Geographical situation and sanitary condition of towns surveyed.—All the three towns are situated in the Aurangabad district in the north-west corner of the dominions, which has an average rainfall of 35.8 inches and a mean temperature of 98.6°. The district is famous for its cave temples at Ellora and Ajanta.

many ginning factories. It has a mean height above the sea level of 1,670 feet. The soil is black cotton soil and morum overlying basalt rock. It is situated on the bank of Kondalki, a minor tributary of the Godavari, which divides the town into two principal parts, north and south. The south is old town, highly congested with narrow winding lanes and in parts with close aggregation of buildings forming insanitary labyrinths which cannot be efficiently cleansed and in

which the air is almost always stagnant. Cattle sheds were frequently found in this part of the town quite adjacent to living rooms. It has a number of old ruins including the fort. It is here that most of the cases of oriental sore were detected.

In the northern part of the town, which includes the cantonment area, better sanitary conditions prevail, though slum areas are not infrequently found where cases of oriental sore were found in fair numbers.

Pattan, also known as Paithan, is the headquarters of Pattan taluq, with a population of 6,294. The town is situated on the left bank of the river Godavari, with 1,500 feet. It was the seat of the empire of the Andhra Kings, but is now reduced in importance. A few stone and brick houses remain from its prosperous days. The sanitation of the place is poor with many dark ill-ventilated houses; hence it is a stronghold of sand-flies. It is a place of pilgrimage due to the temple of Eknath, one of the staunch devotees of the deity of Pandharpur, about half a mile from the town. A *jatra* is held every year in the last week of March when about 40 to 50 thousand people congregate.

Incidence of the disease.—The following statement shows the incidence of oriental sore among the general population examined in the three towns surveyed:—

Town	Number of houses inspected	Number of persons examined	Number of cases found	Incidence rate per mille
Aurangabad	106	1,032	5	4.84
Jalna ..	485	3,242	90	27.76
Pattan ..	315	1,781	76	42.68
TOTAL ..	906	6,055	171	28.24

Age incidence of the cases detected in the three places is shown in the table below:—

Town	0-1 year	1-5 years	6-10 years	11-15 years	16-20 years	Above 20 years	Total
Aurangabad ..	1	2	2	5
Jalna ..	3	35	21	18	3	10	90
Pattan ..	4	39	13	11	2	7	76
TOTAL ..	8	76	36	29	5	17	171

It shows that 70 per cent of cases occur in children below the age of 10. This is again borne out by the high incidence rate among primary and middle school children examined. Recorded figures are tabulated below. The age of children examined did not exceed 12 years.

The incidence of oriental sore among this selected group of population of children in the three towns was 28.45, 74.17 and 116.44 as against 4.84, 27.76 and 42.68 in the general population. This shows a higher prevalence of the disease among children than among adults. This is explained by the fact that those having ulcers in earlier life rarely suffer from a second in the later years; immunity produced appears to last a life time. In view of this fact, prophylactic inoculation with cultures of *Leishmania* has been practised in south-east Russia (Lawrow and Dubowskoj). Sores develop at the site of inoculation after an incubation period of 2 to 6 months. The immunity thus produced protected against further infection. We do not however see any advantage in such prophylaxis when the disease produced by artificial inoculation does not differ from that naturally contracted except that one could choose a convenient time to have the disease (and a convenient part of the body.—Editor).

Sex incidence.—Among a total of 171 cases examined in the general population, 91 or 53.2 per cent were among males and the rest 80 or 46.8 per cent were among females. This slight difference can be easily accounted for by the general tendency among the local females not to come forward for examination. The incidence among both sexes appears to be almost the same.

Situation of the ulcers.—While examining the cases, a careful record was kept regarding the sites affected. A summary of the results is given in the table on page 88.

The exposed parts, such as the extremities and face, were thus more frequently affected than the covered parts, such as the trunk. Cases with

multiple sores were not infrequent, particularly at Pattan and among children, while single sores were the general rule among the adults in all the three towns examined.

Species of sand-flies caught.—In all the three towns surveyed, 940 adult sand-flies of different

Town	Number of schools inspected	Number of boys examined	Number found infected	Incidence rate per thousand	Number of girls examined	Number found infected	Incidence rate per thousand
Aurangabad ..	11	1,511	43	28.45	178	10	56.18
Jalna ..	8	728	54	74.17	199	5	25.13
Pattan ..	3	292	34	116.44
TOTAL ..	22	2,531	131	51.76	377	15	39.78

Sites affected in cases of oriental sore examined

Site affected			Total number of cases found
EXTREMITIES—			
Upper	50
Lower	38
TOTAL	88
FACE—			
Cheeks	40
Lips	11
Eye-lids	1
Ear	9
Nose	6
TOTAL	67
TRUNK—			
Chest	6
Abdomen	2
Back	11
Neck	2
TOTAL	21

species were caught and of this number 483 were females and the rest males. The table below gives the details of the various species caught:—

Town	<i>P. papatasi</i>			<i>P. argentipes</i>			<i>P. antennatus</i>			<i>P. babu</i>			<i>P. bailyi</i>			<i>P. sergenti</i>		
	M.	F.	Total	M.	F.	Total	M.	F.	Total	M.	F.	Total	M.	F.	Total	M.	F.	Total
Aurangabad ..	48	36	84	39	25	64	6	7	13	6	9	15	8	9	17	1	..	1
Jalna ..	133	101	234	40	85	125	5	9	14	4	5	9	2	6	8
Pattan ..	80	90	170	59	69	128	21	24	45	5	8	13
TOTAL ..	261	227	488	138	179	317	32	40	72	15	22	37	10	15	25	1	..	1

Phlebotomus papatasi.—This was by far the commonest species met with during the survey. Of the 227 females caught, 200 were dissected and in two of them (one from Jalna town and the other from Pattan) flagellate infection was detected in the midgut.

Phlebotomus argentipes.—This is the second commonest species of sand-flies found in the towns surveyed. One hundred and thirty-eight males and 179 females were caught. Of the 160 female flies dissected, none was found infected.

P. sergenti.—The solitary male specimen of *P. sergenti* was found at Pattan and was preserved after identification. Further search for sand-flies of this species both at Pattan and other places proved futile.

P. antennatus, *P. babu* and *P. bailyi*.—In the minutus group the largest number found (72) belonged to the species *P. antennatus*, while the other two species, viz, *P. babu* and *P. bailyi*, were represented by the small numbers of 37 and 25.

Breeding grounds of sand-flies.—In order to determine the local nature of the breeding

grounds of sand-flies, an intensive search was made for phlebotomus larvæ. Out of a variety of samples of earth examined from all possible breeding places, two larvæ were discovered in a blend of litter and soil from a cowshed in Jalna. As the larvæ were distorted very much during the process of search, no specific diagnosis could be made. Adult catches from the same area showed only *Phlebotomus papatasi*.

Control measures recommended.—Advantage in control measures should be taken of the breeding habits of the vector. They breed in soil in which there is nitrogenous matter, as supplied by household refuse or domestic animal droppings; in cracks and crevices protected by the overhanging eaves of houses, under trees and bushes, or other heaps of refuse. Proper soil sanitation, the keeping of cattle sheds away from living quarters and, where this is not possible, the keeping of cattle sheds clean by removing the litter to manure pits away from the houses and burning the litter, if it is suspected of actually breeding sand-flies; these are important practical measures.

Spray killing of the adult flies.—Brief experiments carried out in the laboratory have shown pyrocyde mixture, in concentration as used for

killing of mosquitoes, to be equally effective for sand-flies. It is recommended that spraying should be done twice a week as these flies become infective as early as the fifth day after ingesting leishmania bodies (Shortt, Sinton and Swaminath, 1935). Spraying should be vigorous in the affected localities. The fly, unlike the mosquito, has a very limited range of flight, and is therefore nearly always found not far from its breeding grounds; advantage of this fact can be taken in limiting spraying to infected localities or their immediate neighbourhood, special attention being paid to houses where cases have been detected.

Stray dogs with suspicious-looking sores should be destroyed. Sinton has shown that the leishmania occurring on the face of dogs in India are transmissible to man.

The use at night of fine-mesh mosquito netting—40/45 mesh (as against 25/26 mesh used for protection against mosquitoes) is necessary to exclude these tiny insects. An electric fan can also repel the flies. A relative protection from the disease is provided by occupying a bed-room

in the upper stories, as fewer sand-flies are found at higher levels.

Treatment centres to eliminate the source of infection in the affected areas should be started.

Summary and conclusions.—An oriental sore and sand-fly survey of three towns Aurangabad, Jalna and Pattan in the northern part of H.E.H. the Nizam's Dominions was carried out.

The incidence of oriental sore ranged from 42.6 per mille in Pattan to 4.8 in Aurangabad.

There does not appear to be much difference as far as the sex incidence is considered, but the disease is most common among children under 10 years of age.

Six species of sand-flies were found in this area. The most commonly found species were *Phlebotomus papatasi* and *Phlebotomus argentipes*. The other species which were found in small numbers were *P. babu*, *P. bailyi* and *P. antennatus*. A solitary specimen of *P. sergenti* was found in Aurangabad.

Out of 414 female sand-flies dissected, two were found to be infected. Both these specimens (one from Pattan and the other from Jalna) belonged to the species *P. papatasi*.

Control measures are recommended.

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VOGES-PROSKAUER TEST WITH LEIFSON'S REAGENT

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Most bacteriologists held that the old Voges-Proskauer's test (1898) was not a satisfactory test

for the differentiation of the coli-ærogenes group of organisms. During carbohydrate fermentation by the ærogenes group of bacilli, acetoin (acetylmethyl carbinol) is formed, and this is detected by caustic potash and peptone. Acetoin is oxidized to diacetyl, and this reacts with caustic potash and peptone and gives a faint pink colour in the old Voges-Proskauer's test. O'Meara (1931) introduced a more sensitive test by adding creatin which helped to detect acetoin in a dilution of 1 in 20,000 with great ease, and 1 in 50,000 dilution was just capable of recognition. Leifson (1932), by using copper sulphate as a catalyst, introduced a more sensitive test. His reagent was very simple, less expensive, and could be preserved for a long time in a glass-stoppered phial. To 1 c.cm. of culture, 1 c.cm. of this reagent was added and mixed. The reaction was markedly positive, showing bright red or eosin-like colour at the surface in 10 to 20 minutes at room temperature. The maximum time required was 2 to 4 hours. Only two days' old culture in glucose phosphate broth at 37°C. was required. The formula of his reagent is as follows:—

CuSO ₄ , 5 H ₂ O	1 gm.
Conc. am. hydroxide	40 c.cm.
(sp. gr. 0.90).	
NaOH 10 per cent	960 c.cm. to be added last.

The reagent should be kept in stoppered bottles. Barritt (1936) introducing α -naphthol discovered a more sensitive and specific test, and was able to detect acetoin in a dilution of 1 in 1,000,000 in 2 to 5 minutes. But he used 3 days' old culture at 37°C. Seetharama Iyer and Raghavachari (1939) used Barritt's test in bacteriological analysis of water and found it to be specific and highly sensitive. They did not compare the utility of the test with that of Leifson. They advocated carrying out both methyl-red test and Voges-Proskauer's test in succession in the same culture tube. Seshadri-nathan and Venkataswami (1943) carried out Barritt's test on coliform organisms of the urinary tract and confirmed the test as satisfactory, but they also did not compare the test with Leifson's.

We could not procure α -naphthol and creatin, and hence we had to use Leifson's reagent alone in comparison with the old Voges-Proskauer's test, and found the test very reliable. The few coliform organisms that we tested with Leifson's reagent and by Barritt's method showed that the tests tallied with each other. The positive reaction is indicated by the development of a bright red or pink colour in 10 to 20 minutes. The maximum time required is 2 hours. A bluish violet colour or absence of any colour indicates a negative reaction. No reading should be taken on the next day after addition of the reagent. The test should not be done on 3 days' old culture. Our results are given in the following table.

TABLE

Organisms	Number of strains	Voges-Proskauer's test, Leifson's	Voges-Proskauer's test, original	Methyl-red test	Indole	Citrate Koser's
<i>Bact. aerogenes</i> type I	46	+ 46	+ or \pm 31 - 15	-	-	+
<i>Bact. aerogenes</i> type II	4	+ 4	+ 2 - 2	-	+	+
<i>Bact. coli</i> type I ..	39	- 39	- 39	+	+	-
<i>Bact. coli</i> type II ..	1	- 1	- 1	+	-	-
Intermediate I and II	5	- 5	- 5	+	\pm	+
TOTAL ..	95					

The above table shows that in 95 strains of the coli-aerogenes group of organisms, Leifson's test has succeeded and corresponded with methyl-red test and citrate tests, whereas in 50 strains of *Bact. aerogenes*, the old Voges-Proskauer's test has been negative in 17, and this means that the error is high. Our conclusion is therefore that Leifson's reagent can be used as a reliable test. The advantages over Barritt's test are that the reagent is only one, easily available, less expensive and can be preserved in a stoppered phial; the test is more quickly and easily performed and the incubation time required for the test is shorter. In these days it is difficult to get creatin and α -naphthol. So Leifson's reagent can be used instead.

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THE DISTRIBUTION OF TYPHOID VI AGGLUTININS IN NORMAL SERA WITH SPECIAL REFERENCE TO THEIR DIAGNOSTIC VALUE IN TYPHOID FEVER

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ISOLATION of the causative organism from blood, urine or faeces of a patient, remains even to this day an unquestionable evidence of disease such as typhoid fever. However, when that is not practicable, reliance has to be placed on the serological diagnosis using the conventional Widal test, the correct interpretation of the results of which is beset with many difficulties. The discovery by Felix and Pitt (1934) of a Vi antigen of *B. typhosus*, and its serum-counterpart Vi antibody in the sera of typhoid patients and carriers, opened up a new serological

approach to the problem of diagnosis of typhoid infection. Bensted (1937) and many other workers since then have confirmed the findings of Felix and his co-workers and acknowledged the importance of Vi agglutinins in the diagnosis of typhoid carriers; but the demonstration of these agglutinins involved a laborious technique of preliminary absorption of H and O agglutinins, which made it hardly a practical proposition to be used in the routine work. Bhatnagar, Speechly and Singh (1938) overcame these difficulties by finding out a pure non-motile strain of *B. typhosus* Vi I Bhatnagar, rich in Vi antigen and possessing only a trace of O antigen. Using this strain, Bhatnagar (1938) showed the development of Vi agglutinins in acute typhoid cases, whether uninoculated or inoculated, to be very regular, provided the tests were done at proper intervals, during the course of disease. But such repeated examinations of blood, though possible among men under military discipline and in hospitals, could not be done in private practice, and reliance had to be placed on a single serological examination. Under these circumstances, of what value Vi agglutination test could be was not known, and since this Institute was giving free diagnostic aid to medical practitioners, in the diagnosis of typhoid infection, it was decided to take this opportunity to examine such sera for the presence of Vi agglutinins. An accurate knowledge of the limits of natural Vi agglutinins among the local population is essential to the determination of the lowest significant Vi titre, and in view of the paucity of published data on the subject, it was considered desirable to secure information concerning the distribution of Vi agglutinins in normal sera in Bombay population.

Three hundred random samples of blood received for Wassermann reaction were tested for the presence of Vi agglutinins. Only clear sera, free from haemoglobin, were used for the tests. The antigen used was a live suspension of *B. typhosus* strain Vi I Bhatnagar, prepared from a 24-hour culture on saccharose-agar, and the strain was maintained according to the instructions given by Bhatnagar in his paper. The suspension had an opacity of about 8,000 millions of organisms per c.cm. In addition to

this, a preserved agglutinable Vi I suspension from the Enteric Laboratory, Kasauli, was used in parallel, in the earlier part of the investigations. The suspensions, both living and killed, were required to satisfy the criteria of sensitivity to Vi sera in high dilutions and non-agglutinability in pure O and H antisera, even in a dilution of 1 in 5. Dilutions were put up in Felix tubes and ranged from 1 in 5 to 1 in 25 in case of normal sera. Dreyer's drop technique was used throughout, and one drop of the suspension was added to each tube of serum-saline mixture, which amounted to one c.cm. The racks were well shaken and incubated at 37°C. for two hours and were left at room temperature overnight. Readings were taken next morning according to the instructions given by Bhatnagar. Each tube was examined naked eye as well as with a magnifying lens, and the reading was confirmed by gently shaking each tube.

Three hundred samples of normal sera were thus examined for the presence of typhoid Vi agglutinins. The results are set forth in table I.

TABLE I
Vi agglutination in 300 normal sera

Agglutination titre against strain Vi I	Number of sera	Percentage showing agglutination
1 in 5	17	5.65
1 in 10	4	1.35
1 in 16.5	1	0.3
1 in 20	0	0.0
1 in 25	3	1.0
1 in 5 to 1 in 25	25	8.3

The information concerning the distribution of Vi agglutinins in normal sera is very scanty, and among the few workers who have published the reports are Pijper and Crocker (1937), Lewin (1938), Horgan and Drysdale (1940), Davis (1940), Radowsky (1942) in different parts of Africa; Eliot (1940) and Coleman (1942) in U.S.A.; Bhatnagar and his co-workers (1937) in India. The number of normal sera showing Vi agglutinins varied from 2 to 10 per cent, in the hands of different workers, in the absence of any uniformity of technique; the technique varied essentially in regard to the range of dilutions put up, the strain of *B. typhosus* used, for the preparation of suspensions. In this investigation, as pointed out before, a Vi I strain of *B. typhosus* was used throughout, and the technique followed essentially the instructions given by Bhatnagar personally. The results obtained from table I clearly indicated that only in 25 out of 300 normal sera (8.3 per cent), Vi agglutinins could be demonstrated. Seventeen out of 25 such sera were positive in a dilution of 1 in 5 only. It was not possible to obtain any samples of faeces from the Vi positive persons; therefore the significance of the positive findings could not be further

estimated. With 92 per cent of normal sera failing to contain Vi agglutinins even in a dilution of 1 in 5, the minimum Vi diagnostic titre in the serum of a clinically typhoid fever case, was fixed as the 1 in 10 dilution of the serum. A further rise in the Vi titre with the examination of a second sample would establish the diagnosis of the disease.

Fully armed with the proper technique and having secured the necessary information regarding minimum diagnostic Vi titre for the local population, an investigation was carried out on 75 sera of bacteriologically proved typhoid fever cases, as to the presence of Vi agglutinins in sufficiently diagnostic titre. All the cases were uninoculated with T.A.B. vaccine. Only one single sample of blood from each patient was available for testing the serum for the presence of O, H and Vi agglutinins. The clot culture was done in ox-bile as described previously (Soman, 1932). Thus in every case the clot culture was positive for *B. typhosus*. The majority of samples of blood were received during the second week of fever. The technique of Vi agglutination essentially remained the same as described above except that serum dilutions ranged from 1 in 10 to 1 in 200. In the case of O and H agglutinations, the dilution of serum varied from 1 in 50 to 1 in 1,000 and the racks were incubated in the water bath at 56°C. for four hours and then were left in the refrigerator overnight. Readings were taken next morning and the results of Vi, O and H agglutinations were compared as to their diagnostic significance. The results are summarized in table II.

TABLE II
O, H and Vi agglutination in the diagnosis of 75 typhoid fever cases

Total number of cases <i>B. typhosus</i> isolated	Positive by H and O test	Positive by H, O and Vi test	Positive by Vi test only	Negative by O, H and Vi test
75	70	71	46	4
100%	93%	95%	61%	5%

The results clearly indicate the comparative diagnostic value of O, H and Vi agglutination by a single serological examination. Vi agglutinins could be demonstrated in sufficiently diagnostic titre in only 61 per cent of the total number of typhoid cases. If reliance was placed on Vi agglutination alone, in 29 out of 75 cases, the diagnosis would have been missed altogether. While by incorporating Vi agglutination test as a routine along with O and H agglutination; only one more case would have been diagnosed. The combined method of O and H agglutination could help the diagnosis in 93 per cent of cases of typhoid fever. In four cases, no kind of

agglutinins could be demonstrated and the diagnosis was only arrived at by a positive clot culture. Bhatnagar (1938) found the Vi development to be very regular in 134 cases of typhoid fever, inoculated and uninoculated, and since then many other investigators (Green, 1940; Almon and Stovall, 1940; Eliot, 1940; Coleman, 1942) tried Vi agglutination as a routine test in the diagnosis of typhoid fever but the results failed to come up to expectations. They could demonstrate the Vi agglutinins in less than 50 per cent of typhoid cases only. Wagle (1941) in Bombay found the Vi agglutination test to be diagnostic in 67.4 per cent of typhoid cases only, doing a single serological examination. Bensted (1940) found 75 per cent of sera which showed the presence of Vi agglutinins when repeatedly examined at short intervals. Even then in 19 cases he found a complete absence of Vi agglutinins in a serum dilution of 1 in 20 or upwards, throughout the disease. Seshadrinathan and Pai (1940) in Madras could diagnose 77.1 per cent of typhoid cases by Vi agglutination test alone. The results of this investigation however showed that Vi agglutination test on a single sample of blood could be of diagnostic value in 61.3 per cent of typhoid cases in Bombay. As the value of any such tests depended on the practical application in the diagnosis of the disease, it was disappointing that the development of Vi antibody could not be demonstrated in every case of typhoid fever. Under the conditions, the routine combined method of clot culture and O and H agglutination (Soman, 1932, 1934) proved the method of choice for the diagnosis of typhoid fever.

Summary

1. Three hundred samples of sera, sent for Wassermann reaction, were tested for the presence of typhoid Vi agglutinins.

2. Twenty-five or 8.3 per cent of them only were shown to contain Vi agglutinins in titres 1 in 5 to 1 in 25. On the basis of these findings, 1 in 10 dilution of a serum was fixed up as the minimum diagnostic Vi titre in a clinical typhoid fever case.

3. Sera from 75 proved typhoid cases were examined for O, H and Vi agglutination, and the results were compared as to their diagnostic value.

4. Vi agglutination test alone could diagnose 61.3 per cent of typhoid cases while 93 per cent of such cases could be diagnosed by the presence of O and H agglutination. In 5 per cent of cases, the diagnosis was solely arrived at by the isolation of *B. typhosus* from clot cultures, as none of the three antibodies could be demonstrated.

5. In cases of typhoid fever, uninoculated with T.A.B. vaccine and with only a single serological examination available, Vi agglutination test, by itself, was found to have hardly any diagnostic value and was actually inferior in

that respect, to the routine combined method of clot culture and O and H agglutination.

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A Mirror of Hospital Practice

COMA DUE TO MALARIA*

By D. J. REDDY

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Of an Indian Field Ambulance

A SEPOY, aged 25, was admitted to hospital at 10 a.m. on 21st July, 1944, with undiagnosed fever. In view of the rush of battle casualties, he was put down for evacuation but was detected as being too ill and was retained. At 6 o'clock that evening, the patient was reported to be unconscious. I found him lying motionless, unconscious and undisturbed by shell fire near at hand. The eyes were sunken; the pupils were normal and deep reflexes not exaggerated. Kernig's sign was absent and the plantar response was flexor. There were no neurological signs. The rectal temperature was 100°F.; pulse 120, volume good. There was pallor probably due to

* Condensed by Editor, I.M.G.

anæmia. The only other clinical finding of importance was enlargement of the spleen.

The following investigations were then carried out. Blood examination for malaria parasites showed none; urine contained no sugar or albumin; lumbar puncture revealed no abnormality in the cerebrospinal fluid.

Examination having excluded other causes of coma, in spite of the failure to detect malaria parasites in the blood, the diagnosis of cerebral malaria was made, and the patient was treated accordingly. At 7 o'clock that evening an intravenous injection of 6 grains of quinine bihydrochloride was given. At 12 midnight no improvement having been seen the dose was repeated and also next morning at 6 a.m. A fourth intravenous injection was given at 11 o'clock that day, and two hours later the patient's condition was much improved, coma having almost passed off. At this time a blood smear showed a few *P. falciparum* rings, and that afternoon a fifth intravenous injection of quinine bihydrochloride was given; after that the administration was oral. Next day he could sit up in bed and take food, and the following day he was evacuated.

The striking points about this case are the failure to detect parasites in the first three examinations, and the excellent response to intravenous quinine given roughly 6-hourly for five injections, 6 grains at a time, the intravenous quinine being given without very serious symptoms. Intravenous quinine given properly when the indications exist, is by far the best mode of administration of quinine; it is replaced by oral quinine when the stomach is able to tolerate and retain it. This opinion has been substantiated by me in treating 100 patients out of 3,500 malaria cases belonging to one or the other forms of dangerous types of *P. falciparum* infection. In my experience in India as a student and later, intravenous quinine was often condemned as being dangerous. My recent experience as well as the experience of others has disproved this.

My thanks are due to Lieutenant-Colonel A. Hunter, R.A.M.C., for allowing me to publish this case report, and to Lieutenant T. D. Gera, I.A.M.C., who has rendered me immense help in preparing this case report.

INFECTIOUS MONONUCLEOSIS

(GLANDULAR FEVER)

By D. J. REDDY

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A PATIENT, aged 22 years, was admitted for undiagnosed fever.

The patient complained of continued fever with headache for four days. There was no cough. For two days he had noticed glandular enlargement behind the ear and in the neck.

Examination.—The patient looks ill; the neck is full; the throat is not congested and no membrane is seen.

The preauricular, submental, cervical and epitrochlear glands are enlarged and vary in size from that of a marble to that of a small potato. The skin over the glands is free; the glands are not matted. They are not shotty to the feel; but they are tender to the touch. The inguinal glands are enlarged and tender but not matted together. The spleen and liver are just palpable but not tender. There is no visible rash on any part of the body. Other systems show no abnormality.

Blood smear.—There is a preponderance of monocytes which amounts to 82.1 per cent, the rest being polymorphonuclears. Most of the monocytes resemble Turk cells. No immature white cells are seen, and no malarial parasites.

Diagnosis.—There was no evidence of syphilitic infection, and he also does not show any healed scars. Moreover, the nature of glandular enlargement and the absence of associated mucous patches excludes syphilis as the cause of glandular enlargement.

Acute lymphatic leukæmia is also excluded, as no immature cell could be found. The diagnosis of glandular fever was made. The agglutination tests, etc., could not be performed.

A CASE OF SCHISTOSOMIASIS INFECTION CONTRACTED IN INDIA

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and .

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Medical Officer in charge of a Surgical Ward

THE literature at our disposal gives no mention of a case of this disease ever having been reported from India before. We feel therefore that sufficient interest attaches to the case to warrant a short note being published.

Case history

On 16th March, 1944, a Sepoy L. S., I. O. C., aged 19 years, a recruit of only four months' service, was admitted to one of the surgical wards of the Indian Military Hospital, Rawalpindi, for investigation of painful hæmaturia.

At the beginning of his service, he was in Poona for a short period of training, and whilst there he was run over by a lorry. The accident was apparently slight but he was put into a plaster jacket for three weeks. He was quite well after this and was doing his duty until the last day of February, when, in the afternoon at a game of hockey, he was knocked down and injured slightly in the lower abdomen. The next day he noticed blood in his urine, but did not report sick. For fourteen days he had some dull pain in the lower abdomen, and at the end of the penis as the act of micturition ended. The urine was high coloured, and often there was a little fresh blood at the end of the flow.

On admission he was found to be a young, healthy, Sikh. No abnormality could be detected in any system or organ. The first urine he passed after admission was examined and noted to be of fair quantity, and a dark brown colour; specific gravity 1014; a slight cloud of albumin. Microscopic examination of the deposit

revealed numbers of red cells amongst which were a fair number of the ova of *Schistosoma hæmatobium*; some phosphates and oxalates were also present.

On 25th March, 1944, cystoscopy was performed. The region of each ureteric orifice was surrounded by a collection of small raised white points, about a millimetre in diameter. Some of these could be seen to be ulcerated. Leashes of vessels ran from the surrounding mucosa up to the limiting edge of each little papule. The trigone was very congested, and a continuous stream of lotion had to be kept running through the bladder in order that a clear view could be got of the ureteric orifices. The appearances were typical of bladder infection with schistosoma.

The daily urine examination showed large numbers of ova. The stools were negative for ova on all occasions, and proctoscopy revealed a congested, but otherwise normal rectum.

The case was demonstrated before the N. W. Army Surgeon's Conference on 30th March, 1944, and a freshly prepared microscopic specimen of the ova was shown with the case. Colonel J. Rodger had already confirmed our diagnosis from his Egyptian experience of the disease; Lieut.-Colonel Puri, I.M.S., and the District Pathologist, Major Chadda, I.M.S., confirmed the diagnosis, at the conference, from their recent experience of the disease overseas. Many of the surgeons present were able to confirm our opinion from their experience.

The case was now being treated with tartar emetic on the usual lines, and on the advice of those with experience of the condition in countries where the disease is common. After three months he was still passing ova in small numbers at irregular intervals; by 5th August, 1944, he had been symptomless for two weeks and the urine was negative for ova for three weeks. He had twice refused cystoscopy, and now, again refused this examination. As he appeared to be well, he was discharged and told to report for observation once a month. Up to now he is well.

Discussion

This young man came to us after he had had only four months' service, and having never been out of his native district except for the short visit to Poona, and his posting to Rawalpindi. When we saw him the disease was well established in the bladder. The suggestion is, therefore, that here is a case of schistosomiasis contracted in India, with the probability of the infection having occurred in his village. Whether the disease exists there, and has existed there for a long period, cannot be said, but one thing seems to come out of this line of thought, and that is that there must be snails in the local water ponds and tanks, which, given the chance to pick up the miracidium, are capable of nurturing it to the free swimming stage and so infecting man. The same applies to the water tanks around Poona if it is postulated that he contracted the infection there. The importance of finding this case cannot be denied, for it means the presence of snails in India which can act as the intermediate host and propagate the disease. With the prospect of infected troops returning from overseas and supplying the ova, there is a possibility of the disease becoming a common scourge in India. If the disease already exists in India, then the areas where it is prevalent must be sought and mapped at once, for without this knowledge we cannot know whether or not the condition is on the increase

from purely Indian sources, or is being imported from Africa, Burma, China or Egypt. It has not been possible for us to go to this man's village to investigate the state of affairs there, but his full particulars are given here for the benefit of the proper authorities and investigators interested:—

Village : Talapur, P. O. Chamkaur Sahib. Thana : Ropar, Railway station : Ropar, District : Ambala.

We have to thank Colonel J. Rodger, Officer Commanding, Indian Medical Hospital, Rawalpindi; for encouragement and permission to publish this note.

A CASE OF FILARIASIS OF THE EYE

By SHYAM SUNDAR LAL SRIVASTAVA,

M.B., B.S., L.O.

Mian Bazar, Gorakhpur

THE patient, a lady aged 26 years, thin built, looking otherwise quite healthy, came to me with the following complaints:—

(a) As she woke up early in the morning, she saw as if some snake appeared coiling before her eyes.

(b) Severe headache since that time. It lasted for about 15 to 20 days and then subsided a little.

Vision.—Right eye (diseased eye):

6/60 \bar{c} - 1.0 Dsph. 6/24

Left eye:

6/24 \bar{c} - 1.0 Dsph. 6/6

On inspection.—The lids, conjunctiva, cornea, iris and anterior chamber were normal; pupils normal in size and reaction.

Homatropin was later on put, and on ophthalmoscopic examination of the fundus, two filarial worms were seen rapidly moving at the macula. I tried to count the oscillation of the body of the worm and found it to be 100 per minute.

During the last 10 days that she has been under my care, she was given two injections of 1 grain of soamin intravenously, but as yet there has been no change either in the position or morbidity of the worm.

The observations of any other ophthalmic surgeons who might have come across the condition, may be requested, and their suggestions as to the line of treatment will be most welcome.

I acknowledge my thanks to Dewan Bahadur W. K. Koman Nayai who very kindly sent his advice on the case.

[Note.—We sent the above case report to Captain E. J. Somerset, I.M.S., Ophthalmic Surgeon and Professor of Ophthalmology, Medical College, Calcutta, for his comment. He has written a note about it which is given below.—Editor, I.M.G.]

'Dr. Shyam Sundar Lal Srivastava's case would appear to be one of filariasis of the vitreous chamber. The case should be watched in the hope that the worms will come forward into the anterior chamber when they can be removed through a corneal incision. No operation through the sclera is as yet indicated.'

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Indian Medical Gazette

FEBRUARY

PENICILLIN IN THE TREATMENT OF WOUNDS

As penicillin is available now in civil practice, the following details from the Report* drawn up by the Penicillin Clinical Trials Committee of the Medical Research Council may be of interest to our readers. The instructions are however provisional, as experience is still not wide enough.

Natural penicillin is an organic acid; its calcium and sodium salts are used in therapeutics. The former is suitable for local treatment, but not for intramuscular injection, as it may cause local necrosis (this is most probably due to impurities). The sodium salt, more difficult to prepare and less stable and also hygroscopic, is used for systemic administration, but may be applied locally if the calcium salt is not available. In appearance, either preparation is a yellow or brownish-yellow powder, freely soluble in water. More darkly coloured samples are less pure. Potency is expressed in terms of Oxford units per mg. Penicillin is adversely affected by heat and moisture, and it should be stored in a sealed container, if possible in a refrigerator. It is also decomposed by acids and alkalies (hence it is ineffective when given by mouth), metallic salts and alcohol, and should not be brought in contact with antiseptics unless they are known to be compatible. Bacterial contamination must be avoided.

As an antiseptic, penicillin is ideal; it acts in extremely high dilutions, it has almost no local or systemic toxicity, and its action is unimpaired by serum, blood or pus. It is bacteriostatic and not bactericidal. Locally applied, it is immensely superior to the sulphonamides. The principal pyogenic cocci, the clostridia of gas gangrene, the pneumococcus, the diphtheria bacillus, and the spirochaetes of syphilis, relapsing fever and possibly Weil's disease are highly susceptible to it, while all gram-negative bacteria, except gonococci and meningococci, are resistant. Among the former, however, occasional strains of bacteria have been observed with an exceptional degree of resistance. Treatment is often successful even when the infection is due to a mixture of resistant and susceptible bacteria.

Penicillin is issued as powder or in tablets, and it is used in three forms which should be prepared with aseptic precautions:—

(a) *Solutions*.—For local application a stock solution of 1,000 units per c.cm. in sterile distilled

water should be made and stored in an ice chest, but should not be used later than 14 days after preparation. Dilute solutions (250 units per c.cm.) for use in wards should be prepared from stock solution and issued in amounts sufficient only for a single day's needs. For intramuscular or subcutaneous injection, sodium penicillin is dissolved in a small quantity of sterile distilled water, e.g. 15,000 units in 2.5 c.cm. For continuous intravenous drip, the requisite amount of such a solution is added to a bottle of isotonic glucose or saline.

(b) *Powders*.—Penicillin is mixed with sulphonamide or sulphathiazole to give a concentration from 500 to 5,000 units per gramme (the lower strength for burns, the higher for wound prophylaxis). It should not be stored longer than a week.

(c) *Creams*.—These are made by mixing with (i) Lanette wax SX 12 parts, arachis oil 25 and water 55 or (ii) 30 per cent Lanette wax in water. Strength—250 units or more per gramme. Creams may be stored in a refrigerator but should not be frozen. They are not stable and should be used within one week.

Penicillin therapy does not obviate the need for adequate surgical treatment. For local application the *solution* is most frequently administered through a tube inserted into the wound which is closed around it, or the tube may be inserted through a separate stab incision and the wound closed completely. The end of the tube protrudes through the dressing, and the solution is injected, not under pressure, with a syringe (without a needle) twelve-hourly; open wounds may be sprayed with the solution, but the powder or cream is to be preferred. Penicillin in a strength of 1,000 to 5,000 units per c.cm. may be injected into abscess cavities following the aspiration of pus. The *cream* may be used for skin infections, burns or wounds which cannot be closed. It is applied daily or every second day. The *powder* may be used for wounds which cannot be closed, or it may be applied preparatory to closure. A blower is essential, and enough should be applied for the whole surface of the wound to be coloured by penicillin. Application should be made every 24 hours at least.

For systemic administration, intravenous or intramuscular injections may be necessary for extensive and deep-seated tissue infections and for septicæmia, but under present conditions it should not be used if the responsible organism is susceptible to sulphonamide treatment. The sodium salt (15,000 units in 2 to 3 c.cm. of sterile water) may be administered intramuscularly every three hours, or intravenously by drip with saline or glucose solution, 100,000 to 120,000 units being given in this way in 24 hours.

The particular method to be used in any case will depend on the particular type of wounds. For surface wounds and burns, penicillin must reach and remain in contact with the whole of the infected surface. Preliminary surgery may

* War Memorandum No. 12. *The Use of Penicillin in Treating War Wounds*. H. M. Stationery Office, London. 3d. net.

be necessary to eradicate pockets or sloughs. The cream (100 to 400 units per gramme) is most commonly used. The solution (100 to 1,000 units per c.cm.) may be applied by compress, but this is rather wasteful. The powder form (500 to 5,000 units per gramme) is applied by an insufflator; its effect may be shorter than when cream is used. If penicillin reaches every part of the wound, sterility is usually obtained in 36 to 72 hours. This is checked by a bacteriological swab. Treatment is continued for a further two to four days, or until two consecutive negative swabs have been obtained. In *soft tissue wounds*, following the necessary surgical excision, small rubber tubes (the number depending on the size of the wound) are inserted as previously described, and about 3 c.cm. (250 units per c.cm.) are injected into each tube at twelve-hourly intervals. The tubes are left in for 3 to 5 days. Penicillin-sulphanilamide is dusted on to any raw surface after the removal of the tubes. Penicillin cream (250 to 1,000 units per gramme) packed in gauze has been used with success on civilian wounds, including lacerations. For *gas gangrene*, local application alone is useless for established cases, and systemic treatment for three days is recommended. Penicillin does not replace, but only supplements, existing methods of treatment (excision of dead muscle, and the administration of full doses of antitoxin). *Compound fractures* should be closed by suture, if possible, after removal of devitalized tissue, and treated with penicillin by the systemic route for 5 days (*i.e.* about 500,000 units) or even longer. In the presence of gross skin loss or a fair-sized dead space, the wound should not be entirely closed. Local treatment as for soft tissue wounds might also be tried. For *wounds of the eye*, one drop of a solution of 500 units to the c.cm. of saline is instilled into the eye half to one-hourly, after 24 hours 2-hourly and later 4-hourly. Sufficient information is not yet available on treatment of *penetrating wounds of chest and abdomen*, and *head injuries*. In *hæmothorax*, infection can probably be prevented by injection of penicillin solution subsequent to aspiration of blood, and repeating injections if fluid recolects. The suggested initial dose is 15,000 to 30,000 units. When the infection is established, aspiration every two days, with partial replacement with penicillin solution, is recommended. If pus continues to form after sterilization, drainage may be required.

In conclusion, it is rarely justifiable to treat any case with penicillin without making a bacteriological diagnosis, since the outcome depends so much on the nature of the infection. When systemic treatment is undertaken, it is recommended that the blood concentration should be checked. This appears to vary in different individuals on a given dosage, presumably owing to differences in the rate of renal excretion.

R. N. C.

Medical News

COLONEL F. P. MACKIE

COLONEL F. P. MACKIE, I.M.S., died in 1944. We have received the following notice about Colonel Mackie written by Major-General Sir John Taylor, I.M.S.:—

'With the death of Colonel F. P. Mackie a link has been lost with the important phase of development of research in tropical diseases which occurred in the earlier years of the present century. Mackie entered the Indian Medical Service in 1902 taking top place and prizes in both Medicine and Surgery. After service in the military side, which included Younghusband's Mission to Tibet, he took up research work and for the rest of his service was a member of the Medical Research Department of the Government of India although taken for other duties at intervals and on mobilization for war.

His first appointment, in 1908, was as Assistant Director of the Plague Research Laboratory, Bombay (later designated the Haffkine Institute on his own suggestion). He was selected for appointment to the Royal Society's Sleeping Sickness Commission with which he proceeded to Uganda to carry out laboratory investigations in the field as one of a team which made important contributions to the knowledge of transmission by the tsetse fly. On return to India, Mackie was put on special duty to investigate kala-azar in Assam, and many important observations were made and much ground cleared during the three years of his enquiry. With the outbreak of war in 1914 he reverted to military employment and served in Baluchistan, France and Mesopotamia in the latter country as Officer Commanding Central Laboratory, Amara, and later in the Central Laboratory, Baghdad. His services were recognized in despatches and by the conferment of the O.B.E.

On return to India, Mackie acted for a short period as Professor of Pathology, Calcutta University, in succession to Sir Leonard Rogers, before taking up the appointment of Director of the Pasteur Institute, Shillong, Assam, where he was again brought into contact with kala-azar work. He remained in this appointment until 1923 when he was appointed Director of his original laboratory, the Haffkine Institute, Bombay, and this remained his substantive post until his retirement although for short periods he officiated successively as Public Health Commissioner with the Government of India and as Surgeon-General, Bombay, and again as Director, Pasteur Institute, Shillong. It had been intended that Mackie should continue his work in India as Director of a special Commission on cholera but it was not found possible to develop this project at the time and he retired from the Indian Medical Service in 1932.

For a man of Mackie's temperament it was not possible to drop active work and he took up the post of Pathologist to the Tropical Diseases Hospital, London, and later on, in 1937, was made Chief Medical Officer to British Overseas Airways Corporation, an appointment which he held up to the time of his death.

During his service Mackie had come into contact with a great variety of problems of tropical medicine and his knowledge of the laboratory aspects of the subject was very extensive. In addition he had had considerable field and clinical experience and his outlook was a practical one. This made him a very suitable representative of the Government of India at the meetings of the Office International d'Hygiène Publique which he attended on four occasions and also at meetings of the Health Committee of the League of Nations at Warsaw, Paris, Tokyo and Bangkok. He was Chairman of the Plague Expert Commission of the League of Nations from 1927 to 1931.

Mackie made contributions to the literature of Relapsing Fever, Sleeping Sickness, Plague, Kala-azar, Cholera, Dysentery, Enteric Fevers, Schistosomiasis, Sprue, etc. He was a Fellow of both the Royal College of Physicians and the Royal College of Surgeons and held the Diploma of Public Health (Bristol).

Public Health Section

OBSERVATIONS ON MALARIA AND OTHER CONDITIONS SEEN IN BURMA EVACUEES

By R. N. CHAUDHURI, M.B. (Cal.), M.R.C.P. (Edin.).
T.D.D. (Wales), F.S.M.F. (Bengal)

and

M. N. RAI CHAUDHURI, M.B. (Cal.)

(From the Department of Tropical Medicine, School of
Tropical Medicine, Calcutta)

In the early part of 1942, when the fall of Burma seemed imminent, the authorities were faced with the problem of evacuating thousands of people to India. Shipping and aircraft being limited, the only alternative was to open up some overland routes, and this was done as expeditiously as possible. Two of these routes are said to have been mostly used, one *via* Tamu, a large village in the frontier, into the Manipur State, and the other leading from the northern part of Burma through the Hukung valley and the Naga hills direct into Assam.

Although a certain proportion of the evacuees withstood the journey fairly well, a great many of them did not complete the trek; they died on the way, while others arrived in a deplorable state of health. Various official and non-official organizations were started for their accommodation, relief, etc., in different places. In Calcutta, an elaborate arrangement was made for the purpose, and most of the sick persons were sent to different hospitals for treatment. During the period of six months from the middle of April to that of October 1942, 144 Burma evacuees were admitted to the hospital attached to this school, under the care of the senior writer. Observations based on these patients constitute the material for this article. Patients with predominating bowel symptoms, about 15 in number, were admitted under a different physician and have not been dealt with here.

Wherever active warfare is in progress such migrations of refugees are likely to be seen, and it may be of some interest to medical men engaged in medical relief to have a resumé of the main diseases found in such refugees in this part of the world, and of the steps taken to deal with them.

Race.—The series included 89 Anglo-Indians, 20 Europeans, 14 Anglo-Burmans, 11 Chinamen, 7 Indians, 2 Burmans and 1 Persian.

Sex and age.—There were 92 males and 52 females. The youngest patient was 9 months and the oldest 65 years old, the majority (55 per cent) being above 20 years.

Duration of journey.—From the history of the duration of journey (since leaving Burma and

arriving in Calcutta) the patients could be divided as follows:—

Duration (in weeks)	2	4	6	8	10	over 10
Number of cases	2	12	25	39	18	12

Thus out of 108 evacuees nearly 60 per cent travelled from 6 to 8 weeks to complete the journey; the statement of 36 persons being too indefinite they have been excluded.

Diagnosis.—The table below gives their diagnosis arrived at after investigation in the hospital.

Disease	Number of cases
1. Malaria	105
2. Typhoid and malaria	4
3. Fever due to other causes	22
4. Miscellaneous	13

1. Malaria

Both the routes used by the evacuees lay through highly endemic malaria regions, so it was inevitable that malaria would play a major part in the lives of the evacuees, although those who managed to get away before the onset of rains probably did not suffer much from it. A doctor who was in Burma Government service states in a personal communication that Tamu is a highly malarious place. Even in summer he had found the spleen index as high as 80 per cent, and it used to rise to over 90 per cent by December. The foot-hills extending north and south are equally malarious. He himself trekked by the second of the above mentioned routes after crossing the Kachin hills, along with hundreds of evacuees, and says that malaria set in after the first few showers of rain, that the incidence of this disease was very high, and that many of the diarrhoeas and dysenteries were due to algid malaria.

In this series, 109 individuals (75.6 per cent) had active malarial infection, four of them having typhoid as well (*vide infra*). Sixty-three of these cases (57.7 per cent) had *P. falciparum*, 36 (33.0 per cent) had *P. vivax* and 4 (3.7 per cent) had mixed infections. Only 2 (1.9 per cent) had *P. malariae* infection; and the species was not identified in 4 (3.7 per cent), only rings being found in thick films. The following table shows the distribution of patients according to the parasites found in blood with reference to their sex and age.

It appears that there was a preponderance of *P. falciparum* infection in both sexes and in adults, adolescents as well as children.

Clinical features.—It may be interesting to note the incidence of the principal symptoms and signs in the infections due to *P. falciparum*

Distribution of patients according to parasites with reference to sex and age.

Infection	Sex				AGE IN YEARS					
	Males		Females		Up to 12		13 to 20		Above 20	
	Num-ber	Per cent	Num-ber	Per cent	Num-ber	Per cent	Num-ber	Per cent	Num-ber	Per cent
<i>P. falciparum</i> ..	40	61.5	23	52.3	11	50.0	19	61.3	33	58.9
<i>P. vivax</i> ..	18	27.7	18	40.9	10	45.5	11	35.5	15	26.8
Mixed ..	3	4.6	1	2.3	1	4.5	0	0.0	3	5.4
<i>P. malariae</i> ..	2	3.1	0	0.0	0	0.0	0	0.0	2	3.5
Rings in thick film ..	2	3.1	2	4.5	0	0.0	1	3.2	3	5.4
TOTAL ..	65	..	44	..	22	..	31	..	56	..

Clinical features

Infection		SYMPTOMS									SIGNS						
		Fever	Headache	Rigor	Chill	Vomiting	Sweating	Muscular pain	Abdominal pain	Diarrhoea	Enlarged spleen	Enlarged liver	Pallor	Toxæmia	Herpes labialis	Jaundice	Congested eyes
<i>P. falciparum</i>	Number	63	28	12	7	12	13	11	4	7	46	18	9	3	4	2	2
	Per cent	100.0	44.4	19.0	11.1	19.0	20.6	17.4	6.3	11.1	73.0	28.5	14.3	4.7	6.3	3.1	3.1
<i>P. vivax</i>	Number	35	18	12	5	7	7	14	2	2	18	13	0	0	2	0	0
	Per cent	97.2	50.0	33.3	13.9	19.4	19.4	38.8	5.5	5.5	50.0	36.1	0.0	0.0	5.5	0.0	0.0

and *P. vivax* as were seen in the patients on admission. This is given in the table above.

Some of the clinical features deserve special notice :—

Fever.—Three patients were entirely free from fever, although their blood showed parasites in fair number, otherwise the temperature mostly took one or other of the forms as detailed in the following table. The remittent type of temperature was commoner in *P. falciparum* than in *P. vivax* infection.

Type of fever

Type of fever	<i>P. falciparum</i>		<i>P. vivax</i>	
	Num-ber	Per cent	Num-ber	Per cent
Intermittent ..	26	44.1	20	71.4
Remittent ..	33	55.9	8	28.6
TOTAL ...	59		28	

Spleen.—It was enlarged in 71 (65 per cent) patients, the size in 64 with reference to the above two infections being tabulated below.

A perusal of the table shows that in 35 (34.3 per cent) cases there was no palpable enlargement of the spleen. This was present in 73 per cent of *P. falciparum* infection and in 50 per cent of *P. vivax* infection. There was only one case in which the spleen was

considerably enlarged extending beyond the level of the umbilicus.

Liver.—It was enlarged in 33 (30 per cent) cases, being markedly tender in 6 cases. The tenderness subsided with antimalarial therapy.

Size of the spleen

	<i>P. falciparum</i>		<i>P. vivax</i>	
	Num-ber	Per cent	Num-ber	Per cent
Not palpable ..	17	27.0	18	50.0
Just palpable ..	36	57.1	14	38.9
1 to 2 inches costal margin.	8	12.7	4	11.1
Over 2 inches costal margin.	2	3.2
TOTAL ..	63		36	

Others.—Nine patients had diarrhoea, two of them passing mucus with stools. It was due to *P. falciparum* infection in 7 and to *P. vivax* in 2. Their stools were repeatedly examined but no pathogenic organisms were detected. Diarrhoea stopped following treatment for malaria. Pallor of the face was a fairly common feature, being marked in 12 cases (11 per cent). A number of patients had an icteric tinge of the conjunctiva; two had distinct jaundice. Herpes labialis was present in 6 cases (5.5 per

cent). Three patients were admitted in a toxic state with heavy *P. falciparum* infection. Two had congested eyes.

Finding of parasites.—The diagnosis was made by demonstrating the parasite in all except one case. The latter was an Anglo-Indian female patient having fever with typical tertian periodicity, but repeated examinations of thick and thin films revealed no parasites. The fever subsided specifically after administration of quinine. Her husband was in the male ward at the same time, and his blood showed *P. vivax*.

The diagnostic procedure carried out consisted of examination of thick and thin films in every case. For staining of the former we adopted the rapid method recommended by Field. The details of the technique appeared in the *I.M.G.*, vol. LXXIX, page 73. Field advocated one second in each solution; we however obtained more satisfactory results by dipping the film for 3 seconds in solution A and for 1 second in solution B.

Blood picture.—A full blood count was done soon after admission in 38 cases, the hæmoglobin varied from 3.8 (28 per cent) to 17.6 (128 per cent) grammes. The red cell count varied from 1.16 to 6.00 millions per c.mm., while the total leucocyte count ranged from 2,500 to 15,000 per

economize in quinine we started using $7\frac{1}{2}$ grains twice a day for 7 days instead. An alkaline mixture was given half an hour before each dose of quinine as a routine. Children under 12 years were given smaller doses of quinine and cinchona; the dose in grains was calculated as 1 plus half the age of the child in years and given twice daily. The dose of alecrin was 0.1 grammes (tablet) three times a day for five days.

The total daily dose of alecrin for children was according to the following scheme:—

Up to 2 years	..	$\frac{1}{2}$ tablet
" 4 "	..	$\frac{3}{4}$ "
" 8 "	..	1 "
" 12 "	..	2 tablets
" 16 "	..	2 $\frac{1}{2}$ "

Out of 109 patients, 47 had quinine, 36 had cinchona febrifuge and 25 had alecrin. One had a different drug and is not considered here.

The blood of 77 patients was examined for parasites repeatedly during the course of treatment. The parasitological picture with reference to the disappearance of parasites following the administration of quinine, cinchona febrifuge or alecrin is tabulated below, the blood being examined regularly every day till negative for parasite (except crescents) for several days.

Effects of antimalarials on parasites

DRUG USED

The day when blood became negative after starting treatment	Quinine		Cinchona febrifuge		Alecrin	
	Number of cases	Percentage	Number of cases	Percentage	Number of cases	Percentage
Second ..	3	8.9	6	23.1	0	..
Third ..	8	23.5	7	26.9	1	5.9
Fourth ..	11	32.3	6	23.1	7	41.1
Fifth ..	2	5.9	4	15.4	8	47.1
Sixth ..	8	23.5	0	..	1	5.9
Seventh ..	2	5.9	3	11.5	0	..
TOTAL ..	34	..	26	..	17	..

c.mm. Anæmia was present in 27 patients and it was normocytic in most cases. Sternal puncture was done in a few cases and the smear showed parasites, their peripheral blood being also positive.

Treatment.—Specific treatment was started as soon as the diagnosis was made. Three drugs were used namely quinine, cinchona febrifuge and alecrin (a substitute for atabrin supplied by Messrs. Bengal Immunity Co.). Until this time, our routine treatment of a clinical attack of malaria consisted of quinine or cinchona mixture, 10 grains twice a day for 10 days; atabrin and plasmochin were unobtainable at the time for regular use. In order to

The cases in which repeated blood examination was not done regularly have been excluded from the above list. A perusal of the table will show that blood became negative for malaria parasite (except crescents) by the 5th day in 70.6 per cent, 88.5 per cent and 94 per cent of patients treated with quinine, cinchona febrifuge and alecrin respectively.

Control of fever.—The temperature became normal on the third day of treatment in most cases. The effects on fever in 58 *falciparum* and 35 *vivax* infections are analysed in the table below.

In either group the maximum percentage of 'normal temperature' was on the third day,

Control of fever in vivax and falciparum infections

Type of infections	Number of cases	NO FEVER ON						
		1st day of treatment	2nd day	3rd day	4th day	5th day	6th day	7th day
<i>falciparum</i>	58	3.4%	29.3%	32.8%	20.8%	7.0%	3.4%	3.4%
<i>vivax</i>	35	14.2%	23.0%	34.3%	14.2%	8.6%	5.7%	..

and about 86 per cent of patients became afebrile by the 4th day. If the cases in which the temperature became normal on the day the treatment was started are excluded, it will be evident that the fever of *vivax* infection yielded less readily than that of *falciparum* infection under specific therapy by the 4th day. About 14 per cent of cases with either infection however continued to have fever (usually low) even after the 4th day, all being normal by the 6th day in the former and by the 7th day in the latter infection.

Intravenous quinine.—Six patients had heavy *falciparum* infection; they were given quinine (7½ grains in 5 cases and 5 grains in one) intravenously on admission followed by oral administration in usual doses. Quinine bihydrochloride solution was mixed with 20 c.cm. of 25 per cent glucose solution and injected very slowly into the vein, none having any untoward effect whatsoever. Clinical notes of these patients are given in the following table:—

Number	Sex and age in years	Type of fever	Spleen	Liver	Other features	Temperature normal on	M.P. negative on
1	M., 44	Remittent	Palpable	Palpable	Marked pallor, abdominal pain and cough.	2nd day	6th day
2	M., 27	Intermittent.	"	Not palpable	Excessive vomiting	3rd " day	4th day
3	M., 27		"	Palpable and tender.	Blood and mucus with stools, profuse sweating.		3rd day
4	F., 14	Remittent	Not palpable.	Not palpable	Marked pallor, bronchitis	4th day	6th " day
5	M., 28	"		"	Toxic, drowsy, icteric, scanty urine, petechial spots on neck.	3rd day	
6	M., 30	"	"	"	Râles. Dysenteric stools. Intercurrent infection.	?	4th day

2. Typhoid and malaria

As already stated, four of the above patients suffered from typhoid fever as well. One patient (case 1) began with malaria and developed typhoid before his blood became parasite-free; case 2 (and possibly 3) had malarial infection during the period while convalescence was expected. Cases 3 and 4 had it during convalescence. Brief notes of these cases are given below:—

Case 1.—A European male, aged 51 years, came on the 16th June, complaining of fever, severe headache, and sometimes profuse sweating and extreme weakness for two days. The temperature was 101.2°F., the tongue was thickly coated and the ankles were slightly cedematous. The spleen and liver were not palpable. The blood examination showed M.T. rings ++; he

was put on cinchona mixture, and the temperature became normal on the 3rd day, but after two days it shot up again, and as the blood still showed scanty M.T. rings, he was switched on to quinine mixture. The blood became negative next day, but the fever persisted. Blood examination revealed slight leucopenia and moderate anaemia. Blood and stool cultures were negative. Urine contained slight albumin, a few granular casts and some pus cells, sodium chloride content being 1 gramme per litre. The Widal was positive TH 1 in 100, the titre subsequently rising to 1 in 800. The patient continued to have high fever, and was very ill and toxic. The temperature became normal on the 24th day of illness and thereafter the convalescence was uneventful. The interesting feature of the case is that the patient had a fairly heavy *falciparum* infection while he was incubating a typhoid infection.

Case 2.—A Chinese male, aged 27 years, was admitted on 4th July for fever, diarrhoea and indefinite abdominal pain for a week. No obvious abnormality was detected on physical examination. Blood—no malaria parasites, fairly normal count; culture sterile. Widal positive TH 1 in 25,000 and TO 1 in 800 (maximum). Stool—ascaris ova (2,800 per c.cm.). About the 4th week of illness the patient ran an irregular temperature which was at first attributed to some complication such as *Bact. coli* infection, but there

was no such evidence. One day he had a sudden rigor, and the blood showed M.T. rings. The fever subsided readily with specific therapy. It is of interest to note that this patient had a latent malarial infection which became patent about the 4th week of illness, delaying convalescence.

Case 3.—An Anglo-Indian girl, aged 16 years, was admitted on the 28th June with fever for one day. Her general condition was good and no obvious abnormality was detected except lice infestation. Blood for malaria was negative and count was about normal. *E. histolytica* (trophozoites and cysts), hookworm and ascaris were found in stools. *Bact. typhosum* was isolated from blood and stools. The Widal was positive TH and TO 1 in 100, the titre thereafter rising to 1 in 800 and 1 in 400 respectively. The course was uneventful till the 17th day of illness when there was a sudden drop of temperature to 98°F. without any obvious cause, but it shot up to 104°F. without chill within a few hours. There was a similar fall of temperature on the

following day. Subsequently she had high continued fever for a week followed by persistently irregular temperature. Blood for malaria was negative repeatedly, and the urine culture was sterile. She was put on quinine empirically, the temperature being normal on the 3rd day of its administration. After 3 weeks' convalescence while the patient was about to be discharged she had sudden fever with ague, *P. vivax* being found this time in the blood which was controlled by quinine. Points of interest in this case are a fairly sudden onset of typhoid fever, unexplained drop of temperature on two consecutive days during the 3rd week, persistent irregular pyrexia thereafter, responding to quinine given empirically and development of active malaria during convalescence.

Case 4.—An Anglo-Indian girl, aged 19 years, was admitted on the 20th July, 1942, with fever for 10 days, starting with chill and vomiting. She was very pale and anæmic; the liver was palpable but not the spleen. Blood examination showed crescents, hæmoglobin 34 per cent (4.67 gm.), red cells 1.76 millions and a normal white cell count. The sedimentation rate 160 mm. after one hour. Blood culture was sterile but the stool culture revealed *Bact. typhosum*. The Widal tests showed the maximum rise in titre of TH 1 in 1,600 and TO 1 in 3,200. As she had already started taking quinine she was put on it but without any effect. The temperature was normal on the 18th day of illness. After two weeks' convalescence she had a rise of temperature and *P. falciparum* was found in her blood for which she was given quinine. It is of interest to note that this patient was very anæmic. She had apparently malaria and typhoid at the same time, and there was a relapse of malaria during convalescence.

3. Fever due to other causes

This group included 22 cases; 5 patients had dengue; in 6, fever was due to sepsis, one having an abscess in the buttock resulting from an intramuscular injection of quinine given out-side. There were 5 cases of respiratory infections, one of which was due to pneumonia. Two had amebic hepatitis; two patients had short fever for which no definite cause could be found; they were classed as P.U.O. One old woman came in very much prostrated with a history of irregular fever and chill which was attributed to pyelitis; she died a few days after admission to the hospital. P.M. was not permitted. Another patient was admitted with fever and arthritis of both knee joints following an attack of acute dysentery about a fortnight previously. Ten c.cm. of clear fluid was aspirated from one joint. He looked very ill and was in distress, but both fever and arthritis subsided quickly on sulphapyridine therapy.

4. Miscellaneous

Five patients were in a state of extreme debility apparently due to the strain of journey. No other obvious abnormality was detected. With rest and dieting they recovered. Five had peripheral neuritis, the lower extremities being affected in all. They complained of pain in the legs, there was calf tenderness, and knee jerks were lost. Motor weakness was however not prominent. One of them died of sudden heart failure within 3 days of admission. Polyneuritis of beri-beri was considered to be the first possibility, but large quantities of vitamin B₁ injected to these patients did not seem to aff

the rate of progress. All of them had sores on the legs during the journey suggestive of Naga sore. It is possible that these sores were infected with diphtheria bacilli giving rise to neuritis. Of the remaining three patients one had duodenal ulcer, one had nephritis, and the third came in with hæmoglobinuria the case note of whom is given below:—

A Hindu girl, aged 10 years, was admitted on 24th August. The history was that she had fever with rigor and vomiting about 10 days previously for which she was given quinine. After a few days she started passing black urine. There was similar history of fever and passage of black urine following administration of quinine 2 years ago while in Burma. On admission, the patient was gravely ill with a temperature of 102.5°F., pulse 160 and respiration 40 per minute. She was very pale and anæmic. The spleen and liver were palpable. There was hæmic murmur in the heart, and the feet were œdematous. Blood examination showed no malaria parasites and a very marked anæmia. Hæmoglobin 16 per cent (2.2 gm.), red cells 0.92 millions, reticulocytes 31.6 per cent, cell volume 10.5 per cent, MCV 114.2 c./μ, MCH 23.9 γγ, MCHC 20.9 per cent, white cells 4,800 per c.mm., polymorph-nuclears 75 per cent, lymphocytes 17 per cent, large mononuclears 8 per cent, eosinophils nil, sedimentation rate 100 mm. after one hour, van den Bergh test—direct negative, indirect slightly positive, bilirubin content 0.5 mg. per 100 c.cm. The urine was dark chocolate in colour and contained copious albumin but no casts or red cells. The benzidine test was strongly positive. Hookworm, ascariis and trichuris ova were found in stool. The Wassermann reaction was negative. She was put on alkalis, intravenous glucose and extract of vitex peduncularis 10 minims thrice daily by mouth and 1 c.cm. by intramuscular injection. The latter was discontinued as it caused severe local reaction. The urine cleared up and the temperature subsided within a week. Next, for her anæmia she was given 3 injections of hepatab followed by a course of ferrous sulphate, 12 grains a day for 3 weeks. The general condition and blood picture steadily improved, the hæmoglobin rising to 54 per cent (7.4 gm.) on 26th September.

With a view to seeing the effect of quinine she was given a test dose of 5 gr. on 29th September but nothing happened. She had 2 more doses when hæmoglobinuria started but it subsided spontaneously in a couple of days, while the hæmoglobin came down to 44 per cent (6.0 gm.) but got back to the former level in a few days. After a week she was given vitex peduncularis for 3 days and then quinine was given along with it. She had 5 grains once on the first day, twice on the second day and thrice daily for 3 subsequent days while every sample of urine was examined but there was no recurrence of hæmoglobinuria. The patient steadily improved and put on 10 lb. in weight while leaving the hospital. The case is apparently an instance of quinine hæmoglobinuria. The anti-hæmolytic property of vitex peduncularis has been previously reported, but no conclusion should be arrived at from its clinical use in this single case.

Urinary chlorides

To ascertain the salt balance in the body, chloride content of urine was determined in 45 cases of which 22 had 0.3 per cent NaCl or less indicating definite hypochloræmia.

Associated infections

On routine examination of stool and blood, it was evident that a fair proportion of patients had recurrent infection as mentioned below,

the infection being single in some and multiple in others.

	Infection	Number of cases
Stools :	<i>E. histolytica</i> ..	15
	<i>Giardia intestinalis</i> ..	10
	<i>Ankylostoma</i> ..	28
	<i>Ascaris</i> ..	18
	<i>Trichuris</i> ..	18
	<i>Oxyuris</i> ..	2
	<i>Strongyloid larva</i> ..	1
Blood :	<i>Bact. typhosus</i> ..	1
	<i>Microfilaria</i> ..	4

Except one patient with abdominal pain apparently due to ascariasis and another with malaria and amœbic dysentery, none had any definite symptom referable to the associated infection. The patient excreting *Bact. typhosum* was obviously a carrier. Almost all with hookworm and roundworm infection and some with *histolytica* and *giardia* infection were given specific treatment while in the hospital.

Louse infestation.—Thirty-four patients (14 males and 20 females) were infested with lice. They were all deloused by pyrethrum spray.

Summary and discussion

The Japanese attack upon Burma prompted the evacuation of a large population to India in 1942. This necessitated long perilous journey through hilly jungle trails where personal protection against nature, the formidable enemy, was not possible and there was a heavy mortality and morbidity. A study was made on diseases among 144 evacuees admitted under the senior writer. Approximately three-quarter of the cases were malaria, of which 62 per cent was due to *falciparum* infection, reflecting as it does the high incidence of this infection in Burma-India roadway.

Field's rapid method of staining malaria parasites in thick blood films was tried for the first time in this school, and was found with little modification, very satisfactory and economic, the staining being complete in a few seconds and parasites if present being detected very quickly. With the use of this method we could easily examine a large number of films (of old and new patients) daily, and we were so confident about the accuracy of diagnosis of malaria that we invariably withheld giving quinine to those patients showing no parasites. A single exception was a typical case with tertian periodicity in which parasites could not be demonstrated.

Clinical features of the malaria patients were analysed. Forty-seven patients were treated with quinine, 36 with cinchona febrifuge and 25 with alecrin. Fifteen grains of quinine or cinchona a day for seven days supplemented by initial intravenous therapy in severe *P. falciparum* infection was found fairly satisfactory in relieving an acute attack of malaria. The temperature became normal usually after 3 days of treatment, but in a certain proportion of

cases it persisted longer. The blood was however not always parasite-free with the fall of temperature. In the May issue of the *Gazette*, Lowe stated 'there is the commonly held opinion that once a patient has had a few grains of quinine, even if he has malaria, the peripheral blood will often show no parasites. Again and again experiments have shown that even with full doses of quinine the parasites do not usually disappear from the blood for three days'. This is borne out also by the present study.

Four patients suffered from typhoid as well as malaria. It is worth remembering the possibility of this combination in this country because an associated *P. falciparum* infection, if undetected and untreated, may prove fatal, and the death may be wrongly attributed to typhoid. It was not possible to ascertain the relapse rate of malaria in this series as we adopted the policy of 'quick cure and quick discharge' as many patients were due to travel further to reach their destinations. Anti-relapse treatment was advised on discharge from the hospital, which consisted in giving 10 grains of quinine twice daily for two consecutive days of each week for 2 months. A general tonic such as Eastons syrup was also prescribed. The gametocytes persisted in many of the cases due to *P. falciparum* infection, and could not be eradicated for want of plasmodochin. There was one case of hæmoglobinuria apparently due to quinine in which vitex peduncularis was tried.

Among other cases there were five with peripheral neuritis apparently of toxic origin, possibly diphtheritic, following Naga sores and one with acute post-dysenteric arthritis and fever which responded well to sulphapyridine. Associated bowel infections were fairly common. Thirty-four were infested with head lice; but there was no evidence of any louse-borne infection; they were satisfactorily deloused with pyrethrum spray.

Many had skin troubles, mostly being scabies, impetigo or sepsis. Exhaustion and loss of weight was a common feature while a few had œdema of the legs, possibly of nutritional origin, but there were no signs of unmistakable or obvious deficiency. Some patients were markedly hypochloræmic. There were two deaths in this series.

MALARIA PARASITE FINDINGS IN BLOOD FILMS IN RELATION TO MALARIA FORECASTS IN CEYLON

By V. ST. E. D'ABRERA, L.M.S. (Ceylon)

(From the Division of Medical Entomology, Department of Medical and Sanitary Services, Ceylon)

THE examination of blood films taken from patients diagnosed as suffering from malaria at the Government dispensaries at Wattagama and

Katugastota (basin of the Mahaweli Ganga, altitude, approx. 1,500 ft.) was undertaken with a view to studying the incidence of plasmodia throughout a complete year. A malaria outbreak of some intensity had occurred during the period April to August 1939, and from random samples of blood taken at that time, there appeared to be some variation in the relative prevalence of the three parasites—*P. falciparum*, *P. vivax* and *P. malariae* at the inception, peak and close of the outbreak.

The work was commenced in March 1940 and continued until April 1941 with an interruption in November. A total of 948 blood films (thick and thin) were examined during the period. Malaria parasites were found in 370 or 39 per cent of the films, the parasites being distributed as follows:—

<i>P. vivax</i>	..	159-43 per cent
<i>P. falciparum</i>	..	97-26 „
<i>P. malariae</i>	..	114-31 „

The monthly variations in the relative prevalence of the parasites are indicated in table I. The malaria attendance during this period, as indicated by the combined figures for Wattegama and Katugastota, plotted in graph 1, shows that the outbreak in 1940 commenced during the first week of July, reached its peak at the end of that month and dropped to the pre-epidemic level about mid-September. In 1941 there was no seasonal rise, malaria being static.

Significance of results

1. In so far as definite seasons can be said to exist in Ceylon, the data obtained suggest that there is a definite rhythm in the species

3. When the incidence of malaria was low, *P. malariae* infections predominated.

4. *P. vivax* was responsible for the post-epidemic rise. In September 1940, *P. vivax* was 54.5 per cent and *P. falciparum* 21.2 per cent, while at this time there was a small malaria peak recorded. It is suggested that this rise in fever—the post-epidemic peak—may have been due to relapses, a characteristic of *P. vivax* infections.

Graph 1.—Wattegama.

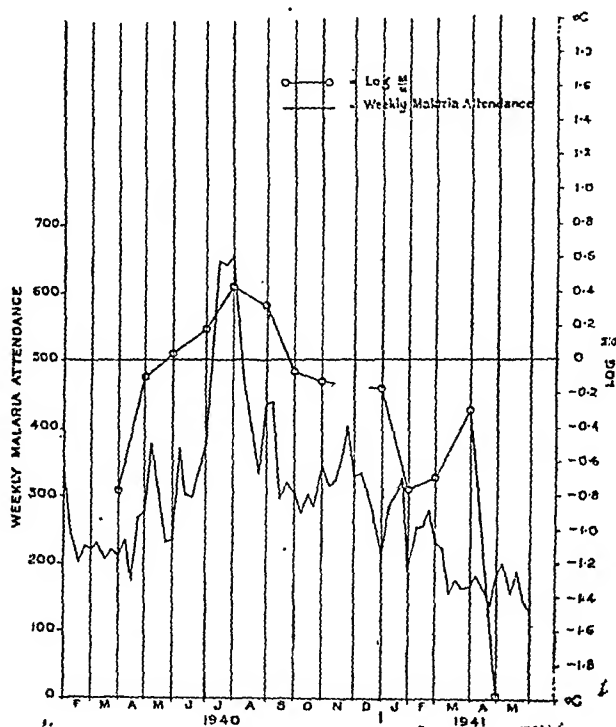


TABLE I

Monthly variation in relative prevalence of malaria parasites, Wattegama, March 1940 to April 1941

Year	1940										1941			
Month	Mar.	Apr.	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.
Number of films examined.	103	183	113	109	90	76	89	34	*	12	55	37	17	30
Number of films positive.	35	73	37	43	44	35	33	10	*	7	17	12	7	7
Percentage with														
<i>P. malariae</i>	51.4	32.8	24.4	27.8	13.6	20.0	24.3	40.0	*	43.0	70.5	41.6	28.6	57.1
<i>P. falciparum</i>	8.6	26.1	27.0	42.0	36.4	42.8	21.2	30.0	*	28.5	11.8	8.3	14.3	Nil
<i>P. vivax</i>	40.0	41.1	48.6	30.2	50.0	37.2	54.5	30.0	*	28.5	17.7	50.1	57.1	42.9
log M/Q.	-0.78	-0.10	+0.04	+0.18	+0.43	+0.33	-0.06	-0.13	*	-0.18	-0.78	-0.70	-0.30	-0.00

* No blood films were taken in November 1940.

incidence of malaria parasites corresponding to the fever seasons.

2. The parasites responsible for the epidemic were *P. vivax* and *P. falciparum*—75 to 80 per cent of the infections.

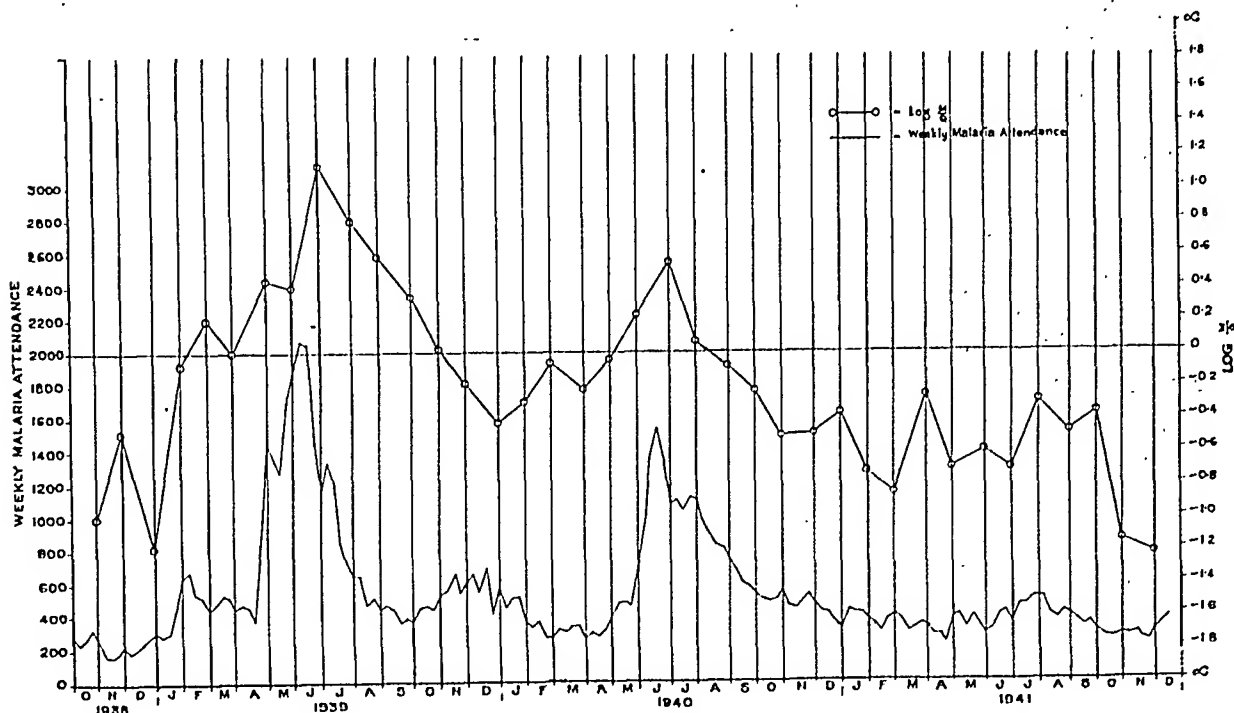
5. Sivalingam (1943a) in a similar investigation in Ceylon at Giriulla (basin of Maha Oya altitude, approx. 200 ft.) during the period October 1938 to November 1941, stated that 'the low relative prevalence of the quartan

parasite on one hand, and a high sub-tertian parasite incidence on the other, appear to be an indication of an approaching malaria outbreak—seasonal rise and epidemic', and suggested that 'an increase of M.T. to 50 per cent or over appears to serve as a warning of an oncoming outbreak of malaria'. He also suggested that

in Ceylon. Carter (Thornton, 1925), Carter *et al.* (1927), Sivalingam and Rustomjee (1941) and Sivalingam (1943b) have all reported on the high incidence of *P. malariae* in the island.

In the two series of observations under consideration, the epidemiological significance of *P. malariae* lies not so much in its dominance

Graph 2.—Giriulla.



'the presence of quartan at 50 per cent or more would seem to be an indication of a healthy season'.

The figures suggested appear to be too arbitrary. In the two rises in malaria incidence shown in the Giriulla series, the highest rates for *P. falciparum* just before the outbreaks were 60 per cent in April 1939 and 40 per cent in May 1940, while in the present series (Wattegama) it was 42 per cent in June 1940. In only one case, therefore, out of the three in question was it possible on the criteria suggested to anticipate the oncoming outbreak, and in this instance the interval between the initial fever rise and the date of forecast was so small, a matter of two weeks only, that it is doubtful if it would have been of any practical value.

The fact that there appears to be some inter-relationship between the parasites, more especially *P. malariae* to *P. falciparum*, is of epidemiological importance, and in Ceylon in rainfall zones where outbreaks of malaria are closely linked up with the vagaries of the monsoon, it would be valuable to be able to state in advance whether an outbreak could be expected. Although Gill (1938) does not consider the prevalence of *P. malariae* of epidemiological importance owing to its alleged rarity, it is an established fact that *P. malariae* plays a very important part in the ætiology of malaria

over each of the other species at any given time, as in its definite reduction in prevalence after a period of such dominance. Therefore, if it could be estimated at what point in the epidemic cycle *P. malariae* begins to give place to *P. falciparum*, it should, besides providing a less arbitrary method for anticipating an outbreak than that suggested by Sivalingam, also furnish a useful time interval between the forecast and the onset of the epidemic which could be put to practical use.

In order to indicate this point, the ratio of the number of *P. falciparum* infections to those of *P. malariae* was calculated, and an attempt made to plot the results, but the graph obtained was found to be unsatisfactory, since when the ratio was less than unity, the variations in the graph were so small that they did not appear to be proportional to the decrease in morbidity. Similarly, when the ratio of *P. malariae* to *P. falciparum* was calculated, the variation in the ratio, when less than unity, did not appear to be proportional to the rise in morbidity. However the point at which *P. malariae* would give place to *P. falciparum* could not be mathematically computed, and this point would yet have to be made arbitrarily. When however the log of the ratios was calculated ($\log M/Q$, where $M = P. falciparum$ infections and $Q = P. malariae$ infections), the resulting graph



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besides being proportional to the rise and fall in morbidity, also provided a zero. Another advantage in this method of calculation was that it gave a negative phase which corresponded to the period when fever was low and static. These calculations have been plotted in graph 1 for Wattegama, and graph 2 for Giriulla (Sivalingam's data). If zero in the graph be considered as the point when *P. malariae* begins to give place to *P. falciparum*, then at the end of February 1939 and at the beginning of May 1940 in the Giriulla series, and the end of May 1940 in the Wattegama series, if a forecast had been made, there would have been intervals of nearly two months, two weeks, and one month respectively before the commencement of the outbreaks. The importance of the negative phase and its value is also apparent in the Giriulla 1941 and Wattegama 1941 periods where

zero was not reached, the curve remaining negative throughout the whole year so that no fever forecast was made.

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Current Topics

Infective Hepatitis

By J. D. S. CAMERON

(Abstracted from the *Quarterly Journal of Medicine*, Vol. XII, July 1943, p. 139)

THE work reported in this paper was carried out at two Army General Hospitals in Palestine during 1940 and 1941, when infective hepatitis appeared in epidemic form among the troops.

The concept of epidemic hepatitis.—There can be little doubt that modification must be made in the original concept of catarrhal jaundice advanced by Bamberger, supported by Virchow and upheld by most physicians until recent years. It was generally maintained that the initial lesion was a gastroduodenitis followed by spread of 'catarrh' to the epithelium of the bile ducts, thereby producing an obstructive jaundice. The same view was accepted by pathologists, and the usually benign prognosis has delayed the elucidation of the true pathology. The occurrence of a biphasic van den Bergh reaction raised doubts about the simple explanation, and suggested that liver damage must be combined with biliary obstruction, if, indeed, the latter was present at all. Many physicians have claimed that two conditions exist—true catarrhal jaundice with the obstructive element predominating and little, if any, hepatic involvement, and infective hepatitis in which liver damage is of major and biliary obstruction of minor importance. The cases discussed in the present report undoubtedly fall into the second category and the term infective hepatitis has been used in preference to catarrhal jaundice. Further, we are of opinion that in some instances hepatitis is present without jaundice occurring at all, although the other clinical symptoms and signs characteristic of the disease are evident.

I. CLINICAL PICTURE

In all, 250 cases have been studied and the following account is based on the clinical records of 170 patients. *Pre-icteric stage.*—After a long incubation period (shown later to be 32 days as a minimum) the disease starts in a way closely resembling sand-fly fever, and in fact this was the initial diagnosis in the majority of the early patients in the epidemic. Fever, malaise, and headache are present in both conditions at the outset, but in infective hepatitis the headache is less intense. Moreover, it lacks the characteristic pain in,

behind, and on movement of, the eyes found in sand-fly fever. Anorexia is invariable and far greater than in sand-fly fever; in fact the importance of the initial anorexia cannot be over-emphasized and is so complete that all food may be refused for two or more days. Disinclination for smoking is also present. Nausea is common, but vomiting unusual. The tongue is clean, but a taste variously described as 'like rubber', 'sour', or 'bitter' is often complained of. Labial herpes was never noticed, a point of difference from spirochætal jaundice. Abdominal discomfort, more a tightness than a pain, was common in the right upper abdomen, and the bowels more often showed a tendency to constipation than diarrhoea. Fever was present in all cases observed during the pre-icteric stage. It was of fairly regular type, varying as a rule between 99°F. and 103°F. (highest 104°F.) and continued for three to six days when jaundice appeared. In a number of cases when the fever abated the patient still remained unwell, and three to ten days later another bout of fever ushered in jaundice. Dr. Btesh of Haifa considers that jaundice more often occurs with the second period of fever than the first, and so has divided the clinical picture into four stages of (1) initial fever, (2) intermediate period, (3) hepatotoxic stage with fever, and (4) jaundice. A few cases showed continued jaundice up to 14 days which did not terminate when jaundice developed. Others showed the initial pyrexia followed by a low fever lasting up to 14 days after jaundice appeared.

Jaundice.—There is a clinical opinion in Palestine that the disease may occur without jaundice at all, but the present description refers to our cases in all of which jaundice was present. The prodromal symptoms already described, continued for one to eight days prior to the discovery of icterus, the average duration of the pre-icteric stage in 170 patients being five days. With the development of jaundice the initial symptoms rapidly subsided, and in many cases appetite returned within four days. Anorexia continued, however, with diminished intensity in cases in which bile remained absent from the stools for longer than usual. Fever ceased as a rule whenever jaundice appeared. The depth of jaundice varied greatly from a light coloration of the conjunctivæ to a deep icterus involving the whole body, and appeared to bear a relationship to the severity of the symptoms. The average duration in 170 cases was 21 days (maximum intensity at five days), but it ranged from 5 to 72 days. Itching was

complained of by only eight patients on admission, but others developed this symptom later. Severe cholæmic symptoms were present in one officer who was very deeply jaundiced, and to a lesser degree in six other patients. Disturbance of visual accommodation was twice reported. Bradycardia occurred as soon as jaundice developed, but this seems to accompany all virus infection and is very noticeable after sand-fly fever. It may be noted that during the pre-icteric stage tachycardia is the rule.

Other symptoms and signs.—Enlargement of the liver was noted in 97 of the 170 patients, the average being to $1\frac{1}{2}$ fingers' breadth below the costal margin, and the largest three fingers' breadth. The enlargement was transient, lasting 7 to 14 days in most cases. In the greatest enlargement of all return to normal was noted after 12 days. Tenderness in the hepatic area was present in 109 cases, associated with liver enlargement in 89 and without enlargement in 20 cases. A palpable gall bladder was detected twice. Splenic enlargement was noted in 46 cases, usually to two fingers' breadth below the ribs, and the organ felt firm on palpation. Hepatic enlargement was found in only 34 of these cases. Our figures, it should be stated, are not in full accord with those of other observers in Palestine, who describe enlargement of both organs in by far the majority of patients. Jossem has stated that 'splenic enlargement varies in degree and is in no relation to the severity of the disease'. In 'the light cases the enlargement is often conspicuous, whereas in severe cases it is even difficult to demonstrate'. The difference in our figures may be partly explained on age incidence, since the vast majority of civilian patients in Palestine are children. Nervous and ocular signs may be expected in a disease strongly suspected as due to a virus. In two patients mental disturbance occurred; in one jaundice was intense and the mental state was attributed to hepatic insufficiency, but in the other the mental disturbance was more severe although jaundice was slight. In three patients temporary ocular difficulty with accommodation was reported, but iridocyclitis (comparatively common in sand-fly fever) was never found. Meningitis, which also occurs in virus infections, was never seen by us, and two cases reported from another hospital were probably cerebrospinal meningitis in which intercurrent infective hepatitis developed.

Urine examination.—Bile was present in all cases, generally appearing on the day prior to the clinical recognition of jaundice. The average duration was nine days, excluding three patients with very prolonged jaundice. Urobilinuria may be noted in the pre-icteric stage and again when biliruria has ceased. During the febrile stage albuminuria is frequent, but never for longer than four days, and tube casts and blood cells were never found. The urinary sediment from 40 cases was injected intraperitoneally into mice to exclude leptospiral infection. All results were negative.

Fæces examination.—In most jaundiced patients the first stool passed after admission was light-coloured, but in some was normal. The stools became clay-coloured in about half of the patients, but in 12 were reported as normal throughout the illness. The average duration of light-coloured stools was eight days, excluding three prolonged cases. Fat analysis of a typical stool at the light stage gave the following result: Total fat in dried stool 46.7 per cent, free fatty acids 30 per cent, combined fatty acids 16.7 per cent. Bacteriological examinations, both during the light- and normal-coloured stages, were all negative. Many cases of jaundice in Gallipoli during the last war were associated with paratyphoid B infection, but this organism was not found, nor did agglutination tests in 40 consecutive cases support this hypothesis.

Blood examination.—Leucocytosis was never found; on the contrary, leucopenia was present in many cases, but not in all. Differential counts showed an invariable neutropenia. The absence of leucocytosis at any stage was regarded as additional evidence against spirochaetosis ictero-hæmorrhagica.

Other tests.—Many additional clinico-pathological tests were carried out, including tests for liver efficiency, blood coagulation time, bleeding time, and blood sedimentation rate; all were within normal limits.

Histamine test.—This test, introduced by Klein for the diagnosis of latent jaundice, proved a valuable help in the diagnosis of the pre-icteric stage of infective hepatitis, and was often positive two to three days before visible icterus was noticed. The test consists in the intradermal injection of 0.25 c.c. of a suitable histamine preparation into a clear area of skin, the inner aspect of the forearm being generally chosen. In the normal subject a characteristic wheal ensues with a white centre. In the pre-icteric stage of hepatitis the hyperæmic edge of the wheal is yellow within $\frac{1}{2}$ to 1 minute, and the whole of the wheal is soon uniformly yellow.

Incubation period of infectivity, and contact infection.—All patients were asked to give a list of close contacts in their unit, and this was compared with all other lists and the names of previous sufferers from the disease. In a remarkably large number of instances contact was readily established, and moreover chains of cases of infection in various units were quickly recognized. From this evidence a tentative minimum incubation period of 32 days was arrived at. It was soon evident that a much longer incubation period must be allowed for in many cases, if the contact assumed to be the source was correct. The hypothesis was made that in such delayed cases the liver was resistant at the time of infection, but later became suitable soil because of some accessory factor such as alcohol, other illness, chill, low diet, or fatigue. The occurrence of hepatitis in the course of some other disease was frequent, wounds, appendicitis, malaria, cerebrospinal fever, diphtheria, and scarlet fever all providing examples. There was also a heavy incidence of the disease following periods of active service in the field. Two interesting examples of contact infection are worth description in full. A private shooting camp was maintained in one area of Palestine, and between 30th September and 6th October this was used by four officers from different units who had not previously met. They were accompanied by three servants and an Arab interpreter. All dispersed to their units on 6th October. One officer was admitted to hospital with infective hepatitis on 2nd November, one servant on 5th November, and the three remaining officers on 6th November. A second servant became jaundiced during December, and as far as is known the remaining servant escaped infection. The Arab interpreter could not be traced. In this series the incubation period appears to vary between 28 and 38 days, except for the servant who fell ill two months after contact.

The second series, illustrating the chain spread of infection, occurred in the staff of the hospital in which our work on infective hepatitis was done.

It was noted that all but one had direct and close contact with a source of infection and that spread from one hospital to another apparently ensued. The occurrence of the disease in a nursing sister and two orderlies engaged in the care of cases of hepatitis is of significance in showing the contagious nature of the disease and the need for isolation of patients. The period of infectivity is obviously important, and although no positive statement can be made, the study of hospital incidence strongly suggests that infection may spread during part of the incubation, the pre-icteric, and a portion at least of the icteric stages. Metsch, in Palestine, states that 'the patients continue to be infective for a long period, even after all traces of jaundice have disappeared'.

Diagnosis.—The diagnosis presented no difficulties in the epidemic circumstances in which our study was made. Five points were recognized to be of major importance in the diagnosis during the pre-icteric stage, and allowed early isolation: (1) anorexia, (2) abdominal discomfort, with or without hepatic enlargement

and tenderness, (3) absence of leucocytosis, (4) increased urobilinogen in the urine, and (5) the histamine wheal test for latent jaundice. In differential diagnosis the chief difficulties were sand-fly fever, during the early pre-icteric stage, and malaria. In the latter disease it should be noted that infective hepatitis has been observed as an intercurrent infection. The diagnosis from spirochaetosis ictero-haemorrhagica presented no difficulty, in the absence of leucocytosis and renal signs, although the positive tests (excepting inoculation of mice with urinary sediment) were not available to us. Obstructive jaundice, with its many causes, was excluded by clinical observations.

Prognosis.—No deaths occurred in the full clinical series observed by us, and in most of the patients recovery was complete in 35 days. A few continued beyond six weeks, and in three patients the duration was over 70 days. Relapse occurred in two patients about a month after discharge from hospital, and no genuine second attacks were met with. The latter point is in accord with the opinion held by civil doctors in Palestine that one attack confers immunity.

Treatment.—Isolation of the patient must be insisted on as far as possible because of the evidence of infectivity, and on our view that lowered resistance of the liver predisposes to infection there should be no mixing with other acutely ill patients. The essence of treatment lies in recognition of the fact that this is a liver disease and not a skin coloration, and a minimum of one month in hospital was found necessary in the mild cases, even although jaundice had disappeared much earlier. No patients were allowed out of bed for at least a fortnight, and disappearance of pyrexia, return of appetite, and fading of icterus, evidence of complete recovery of hepatic function. The patient's appetite was taken as the guide and a diet containing high carbohydrate, liberal protein, and normal fat was reached as early as possible. The presence of clay-coloured stools was held to be the only justification for a diet low in fat and cholesterol, and where the stools remained persistently pale, bile salts were given so that fat could be introduced with the diet. Haemorrhage did not occur in any patients of our series, but in view of the haemorrhagic lesions found in fatal cases we made use of all possible natural sources of vitamin K, since no special preparations were available. In a later case, seen in India, epistaxis occurred every time the patient sat up for any length of time, but this ceased immediately after the intravenous injection of vitamin K. All patients were instructed to abstain from alcohol for a minimum period of three months, on the view that alcohol lowered the resistance of the liver and that the hepatitis might be incompletely healed.

II. GENERAL LABORATORY EXPERIMENTS

Samples of blood were withdrawn from patients as soon as possible after a diagnosis of hepatitis had been made, and included some from the pre-icteric pyrexial stage, the icteric pyrexial stage, and the later icteric non-pyrexial stage. Part of the blood was allowed to clot, but sodium citrate was added to the larger portion to prevent clotting. Samples were taken to the laboratory in thermos flasks over ice. Some animals received whole blood or plasma without further treatment. In others a leucocytic fraction was prepared by centrifugalizing the citrated blood for an hour, the resulting sediment being then suspended in saline and injected. Only young laboratory animals were employed, a number of them being previously starved.

Two to four 'passages' were made from all the animals, except the monkey, the same routes being employed, while passage was also attempted from guinea-pig to mice and from dogs to guinea-pigs. Injections were also made into chick embryos at the fifth day of development (four experiments) and thirteen day (five experiments). From later cases of human hepatitis nasal washings were also taken in normal saline and injected as follows:

- (a) unfiltered, intraperitoneally and intranasally into mice;
- (b) filtered, intraperitoneally and intranasally into mice;
- (c) filtered, intracardially into guinea-pigs.

Passages from these animals were made as before. Careful clinical observations, blood counts, and temperature charts (of the monkey, guinea-pigs, and dogs) were made, but all the experiments must be reported as completely negative. In the guinea-pigs, however, in all of them a leucopenia appeared 5 to 20 days after injection, and one animal showed necrosis of liver cells and round celled infiltration of the portal tract. In a control series injected with normal blood and normal liver the same blood changes were found, but no liver lesion.

Horse experiments

The occurrence of jaundice in horses raised the necessity of excluding piroplasmosis as a cause of the human hepatitis. Human patients were questioned about infestation with ticks, but no evidence was found. Injection experiments from human cases of hepatitis were carried out in six horses. All the experiments were negative.

Human experiments

A call was made for volunteers to be inoculated with blood from jaundiced patients, and an immediate response was obtained from one cavalry regiment and later from another which, however, was prevented from participating by service conditions. Seven volunteers from the first unit were used. Careful clinical examination, investigation for possible contact, and complete blood examination preceded the experiments in which 1 or 2 c.c. of 'infected' whole blood or serum were injected intramuscularly into the buttock. The volunteers were kept under constant supervision by the regimental medical officer and reported to us weekly for examination and blood count, until active service prevented their attendance. It was intended to continue the experiments with filtered serum, nasal washings, and salivary washings in an attempt to establish a virus infection and in the hope of discovering its mode of dissemination, but while these initial observations were in progress deaths from human hepatitis began to occur, and a study of the human pathology (described in Part III) deterred us from continuing the human experiments. Of the seven volunteers inoculated, one was transferred to a special field duty at a distance, and was lost sight of. Of the remaining six, one developed jaundice one month after injection, a second within two months, and the remaining four within six months. The details of the first case are given in full:—

Volunteer I

30th December, 1940. Received 1 c.c. of unfiltered blood serum intramuscularly, the serum being obtained from an apyrexial case of infective hepatitis on the second day after jaundice developed.

29th January, 1941. In the evening anorexia, headache, and mental depression.

30th January, 1941. Above symptoms increased, with fever and pain in the back.

3rd February, 1941. Symptoms unabated. Jaundice appeared.

4th February, 1941. Jaundice increased. Pyrexia ended. Felt better, but marked anorexia, stools pale.

18th February, 1941. Jaundice disappeared clinically, but icterus index was still 20.

The liver was enlarged 1 inch below the costal margin from 1st February, 1941, to 13th February, 1941, but the spleen was never palpable. After discharge from hospital, this volunteer returned to full duty with his unit, and remained well. He died of wounds received in action in June 1941.

Blood and nasal washings were taken from volunteer I, and injected into volunteer II. Up to six weeks after injection no illness followed, when the man left on

active field service. Of the five other volunteers injected with 1 c.c. of blood serum or 2 c.c. of whole blood from infective hepatitis in the pyrexial stage, all were observed for periods up to six weeks, but they then proceeded on field operations. During the next six months, while under active service conditions, all developed jaundice. No full observations could be made, but the histories of their illnesses seemed typical of infective hepatitis. The first fell ill after one month on field service, the last just under six months after injection. This last case was severe, being icteric from 30th August, 1941, to 14th September, 1941. He was seen by us some time later, and gave the following account of himself: 'A month after the injection I felt out of sorts and passed dark urine. I saw the regimental medical officer, but there was no need for hospital. I stuck it out well during the hard marches of the campaign, but just when it was over I went and got the jaundice.' During their period in the field a number of other cases of infective hepatitis occurred in the same unit, but the incidence was low, specially compared with 100 per cent as in the six volunteers. In commenting on these results, we fully realize that the experiment is not a perfect one. While, therefore, it cannot be stated with certainty, it seems probable that the six volunteers who were traced suffered from jaundice as a result of the inoculations, and that in five of them the onset was delayed until the hard conditions of field service rendered them susceptible to the disease. We must also admit the unfortunate fact that these five men may have been the innocent cause of other cases in men exposed to chill, fatigue from long marches, and low rations.

Human experiments with insect vectors.—The worldwide distribution of the disease makes insect transmission unlikely, and the waves of incidence do not coincide with any exacerbation of insect pests. All experiments with insects were negative.

III. THE PATHOLOGY OF HUMAN INFECTIVE HEPATITIS

Personal observations.—Our own observations in the present war concern autopsy material from four fatal cases of acute hepatitis, none from our own clinical series, and all with rather different clinical courses. In addition, we obtained biopsy material from a non-fatal case operated on for an intercurrent subacute appendicitis.

Pathology. Macroscopic.—In four cases the liver was not greatly altered in size, but in the fifth case it was diminished to two-thirds.

Histology.—The microscopic changes in four cases were similar, and were those of subacute necrosis (yellow atrophy) in varying stages. No mitotic figures or evidences of regeneration were observed. The changes in the biopsy material from one case are worth separate description. They consisted of early degeneration in cells at the centre of the lobules, shown by swelling, rounded shape, and diminished intensity of staining; all the degenerating cells showed numerous yellow particles of bile in the cytoplasm; the peripheral cells were normal; greatly increased cellularity of the portal tracts, with lymphocytes and mononuclear cells predominating; Azan staining showed the presence round the central vein of the lobules and in the portal tracts of the hyperplasia of reticulin fibrils described by Iversen and Roholm.

Other pathological changes.—In two patients extensive hæmorrhages were found, and among the areas involved were the subcutaneous tissues, pleura, peritoneum, mediastinum, lungs, heart muscle, subarachnoid space, spleen, kidney and stomach. The biliary tract was particularly examined in two cases, but nothing abnormal was found macroscopically or microscopically. The enlarged spleen was examined in four cases, but nothing beyond intense congestion of the sinusoids (and areas of hæmorrhage in one instance) was found. In two cases the heart muscle showed multiple small foci of hæmorrhage and degenerative changes in the walls of blood vessels. The main conclusion arrived at from the pathological study is that a generalized

infection damages blood vessels, leading to hæmorrhages, and especially to liver damage resulting in necrosis.

SUMMARY AND CONCLUSIONS

1. An epidemic of infective hepatitis is described in soldiers serving in the Middle East. The work is presented in three parts, clinical, experimental and pathological.

2. The work on soldiers has been amplified by correlation with the previous experiences of civilian observers in Palestine, in which the following points seem important:—

(a) The disease in a mild form is common in children in Palestine. One attack leads to immunity, so that few native adult sufferers are seen.

(b) Each immigration of settlers furnishes a new non-immune population, and is followed within a few months by fresh cases of hepatitis, both in children and adults.

The arrival of our troops provided the same set of circumstances, and it is obvious that the mixing of new with seasoned troops may lead to fresh outbreaks.

3. The minimum incubation period is about 32 days, but in many patients is obviously much longer. It is suggested that the incubation period is determined by some additional factor which renders the liver susceptible, such as another disease (sand-fly fever in Palestine), or chill, fatigue, and low diet in field operations.

4. No proof is provided, but the infection is believed to be a virus. Attempts to transmit the disease by insect vectors were negative and direct spread by droplet infection at close quarters requires further investigation.

5. Experiments on the direct transmission of the disease are recorded. These were negative in all animals available, but positive in soldier volunteers. It is admitted that the human experiments were by no means complete and free from possible error, but the reason for their termination is explained.

6. The importance of treating the condition as a serious liver disease is emphasized. In all our patients jaundice of varying degree was present, but other evidence from Palestine seems to show that jaundice is not essential and that a subdivision into hepatitis *cum ictero* and *sine ictero* may be justified.

7. The pathology of four fatal cases, and of a biopsy specimen of liver obtained at operation, are discussed.

A Case of Aspirin Poisoning

By A. D. CHARTERS, M.D., D.T.M. & H.

(From the *British Medical Journal*, i, 1st January, 1944, p. 10)

Records of aspirin poisoning are uncommon enough to warrant publication of a further case.

CLINICAL HISTORY

The patient was a European woman, aged 46, living in Kenya Colony. She had been worried about domestic trouble, and had suggested in a letter to a friend that she was about to commit suicide. On 24th November, 1939, she took 30 gr. of medinal, but awoke from its effects at 8 p.m. On 25th November, at 2 a.m., she swallowed 750 gr. of acetylsalicylic acid (150 5-gr. tablets of Howard's aspirin). The time of taking the drug was ascertained by the patient's personal admission after her recovery, and the exact dosage was proved by counting the remaining (350) tablets out of a previously unopened 500-tablet bottle. There was no vomiting.

I was called to see the patient 14 hours after she had taken the drug. She was sitting in a chair. She was drowsy and disorientated for time, repeatedly mistaking the day of the week. She complained of tinnitus, requesting that the kettle be removed from

the fire. Her respiration was rapid (40 a minute) and deep. Her pulse was 130 and the volume small. She was sweating and complained of the heat, in spite of the fact that the day was cold. She was not cyanosed and had no rash. Her pupils were small and reacted to light. Her reflexes were normal. An examination of the heart and lungs revealed no abnormality. Her tongue was clean.

A catheter specimen of her urine was of normal colour and had an odour of acetone. Its specific gravity was 1030. The reaction was very acid, the pH ranging from 4 to 4.3. The addition of perchloride of iron produced a deep violet colour. Rothera's nitroprusside test for acetone bodies was strongly positive. Gmelin's test for bile pigments gave a positive result. A moderate cloud of albumin was present on boiling. There was a marked reduction of Fehling's and a slight reduction of Benedict's solution. The yeast fermentation test was positive. After 16 hours of yeast fermentation the specimen was again examined for reducing substances, when it was found that, while still producing the same pronounced reduction of Fehling's solution, it was now negative to Benedict's test. This proved that, whereas the reduction of the copper solutions before fermentation had resulted mainly from the presence of salicylic acid, there had also been a trace of glucose. Microscopical examination revealed the presence of several red blood corpuscles and pus cells, but no casts. In order to test the antiseptic action of the drug, a nutrient agar slope was inoculated with a sample (not a catheter specimen) of her urine. No colonies resulted after incubation.

There was a steady improvement in the patient's condition. Her progress is summed up in the following table:—

assistance, one or other of the following diseases might have entered into the differential diagnosis.

1. The combination of respiratory distress with tachycardia has to be differentiated from the dyspnoea of cardiac or respiratory origin. The absence of cyanosis and of abnormal clinical signs in the chest should serve to exclude any thoracic disease, though the presence of pyrexia might at first suggest the possibility of some infective illness.

2. The association of hyperpnoea with the presence in the urine both of acetone and of a reducing substance resembles a ketosis of diabetic origin, but the latter diagnosis is eliminated by the ferric chloride test for aspirin and by the yeast fermentation test, which demonstrates that the main reducing substance is not glucose. The diagnosis can be confirmed, if necessary, by a blood-sugar estimation.

3. Dyspnoea and signs of kidney damage also occur in renal asthma, but the absence of other signs of uræmia, together with the presence of aspirin and salicylic acid in the urine, should readily differentiate the two conditions.

4. The mental symptoms, pyrexia, and respiratory disturbance may simulate a form of infective encephalitis, but the specific urine tests should clinch the diagnosis.

TREATMENT

The main principles of treatment in this case were as follows:—

Elimination of the poison.—(a) Gastric lavage was performed with sodium bicarbonate 1 dr. in one pint of water, after which about 5 oz. of the solution was left in the stomach. As the patient was not seen until 14 hours after taking the drug it is doubtful if this treat-

TABLE OF PROGRESS

	1st day	2nd day	3rd day	4th day	5th day
Temperature ..	Up to 99.4°	Up to 99.2°	Normal
Pulse ..	130 and small	66; normal tension and volume.	Normal
Respiration ..	40 and deep	28	24; varies in rate.	Normal	..
Mental condition ..	Disorientation and drowsiness.	Orientation normal still drowsy.	Still drowsy	Not drowsy	..
Liver ..	Not palpable	Not palpable	Not palpable	Not palpable	Palpable but not tender.
Urine:					
Rothera's test ..	++	++	—
Reduction of Fehling's solution.	++	++	—
Reduction of Benedict's solution.	+	+	—
Ferric chloride test for aspirin.	++	++	++	++	Faint violet.*
Volume ..	Oliguria for 27 hours, during which, apart from one catheter specimen, there was no passage of urine.				

* Further specimens unobtainable owing to recovery and discharge from hospital.

DIFFERENTIAL DIAGNOSIS

Apart from cases of idiosyncrasy, such a large dose of aspirin is required to produce toxic symptoms that poisoning by this drug is nearly always the result of attempted suicide, which may be accompanied by an effort to conceal the cause of the illness. In this particular case the evidence of witness, combined with the presence of the aspirin bottle at the bedside, greatly aided the diagnosis, but, in the absence of such

ment can have been of much benefit. (b) She was given aperients. (c) She was encouraged to take as much fluid as possible, in order to hasten excretion of the drug by kidneys and skin.

Neutralization of the acidosis.—Sodium bicarbonate 30 gr. was administered every two hours.

Abolition of the ketosis and treatment of the toxic hepatitis by insulin and glucose therapy.—The treatment was begun on the second day with an-

injection of 40 units of insulin, combined with oral administration of 40 g. of glucose. This was followed by 20 g. of glucose every two hours for 12 hours. She was then given injections of 10 units of insulin morning and evening half an hour before meals, followed in each case by 40 g. of glucose three hours later.

A diet of high carbohydrate (with low protein and fat) content, in order to assist recovery from the hepatic damage and to avoid further strain on the kidneys.

Lumbar puncture was not performed, but a perusal of the literature reveals that Dyke and Neale record cases of benefit from this treatment, the former also reporting a purple colour on the addition of iron perchloride to the cerebrospinal fluid.

COMMENTARY

Clinical signs.—(1) There was a latent period of about 14 hours between the taking of the drug and the onset of severe toxic signs. This phenomenon has also been observed by Neale and by Biddle. (2) The patient suffered from a mild pyrexia, which appears to be a common symptom, having been recorded by Neale and by Dyke. (3) The most characteristic sign was her marked hyperpnoea, associated with a strongly acid urine. It was caused by acidosis, presumably resulting from (a) the direct action of the acid radical of the acetylsalicylic acid, and (b) disordered metabolism, as exemplified by the acetone in her urine. The difference of opinion over the relative importance of these two factors has been discussed by Dyke, who points out that, whereas Quinke attributes the hyperpnoea to the direct action of the drug, Balázs considers that the sign occurs only in the presence of acetone in the urine. (4) Another feature was disorientation, which might be expected to occur in an organic reaction type of mental disorder. With the exception of drowsiness, no other mental abnormality was present, but symptoms such as restlessness, delirium, and terminal convulsions have been reported by several writers. (5) That the poison caused a toxic hepatitis was shown by the hepatomegaly and by the presence in the urine of bile, acetone, and a trace of glucose. There was no jaundice. (6) There was also evidence of toxic damage to the kidneys; for, as stated above, the urine contained albumin, blood and pus cells. (7) The oliguria—a symptom also noted by Andrews—was probably secondary to the excessive perspiration. There was no evidence of dehydration, though this sign has been observed by Neale, Biddle, and Dyke.

Course.—A study of the table of progress will show that there was considerable delay in complete excretion of the aspirin, the iron perchloride reaction being still slightly positive four days after the taking of the drug. Recovery after such a large dose of aspirin as 750 gr. must be uncommon. Neale records two fatalities after 200 gr. and 750 gr., respectively, and Biddle cites a case of death after 500 gr. Evans describes a case of recovery after a dose of 1,500 gr., but his account suggests that he reached the patient soon enough to be able to hinder absorption by inducing prompt emesis, followed by gastric lavage.

Prostigmin in the Treatment of Delayed Period

By E. FRIEDMANN, M.D., L.R.C.P.

(From the *British Medical Journal*, i, 1st January, 1944, p. 11)

FROM 1940 several papers have been published in America and by workers from the Continent on the action of prostigmin on delayed period; and although the results seem very promising no reports have as yet appeared in this country. This drug made by Roche Products Ltd. has been given an extended trial at the Royal Free Hospital, and its effects on 90 patients are recorded below. It is claimed by those workers that prostigmin invariably precipitates the menstrual flow in all cases of recently delayed period not due to endocrine dysfunctions, systemic disorders or pregnancy.

Their second claim, that it is consequently an alternative to the Friedmann test with regard to its accuracy, is not dealt with in the present paper.

MODE OF ACTION

According to the above-mentioned workers, 'hyperæmia is probably an important and constant factor in menstrual bleeding'. This hyperæmia (a) is a result of oestrogenic action on the uterus, and coincides with the property of the hormone of liberating acetylcholine thus producing vasodilatation; and (b) is under the influence of the parasympathetic nervous system. This being so, it is easy to understand why physical, mental, and emotional upsets, and causes still undiscovered, by altering the parasympathetic control, give rise to a non-endocrine form of amenorrhœa in about 60 per cent of cases. Coincident with this the diminished formation of acetylcholine within the uterine tissues causes a lack of vascular response. This deficiency could be rectified by the administration either of acetylcholine itself or, better still, of a chemical agent such as prostigmin which potentiates the naturally occurring acetylcholine in the uterine endometrium by inhibiting acetylcholinesterase, as in the treatment of myasthenia gravis. It is thus possible to produce hyperæmia similar to that following oestrogenic action without the ill effects which may result from the further addition of acetylcholine.

DESCRIPTION OF TREATMENT

Choice of patients.—'Unsuitable patients' were those with obvious endocrine disturbances, a history of long-standing amenorrhœa, or obvious menopausal symptoms though the menstrual delay was relatively short. Nine such patients were treated without success, and were not included in our series of 90 cases. The ages of the patients varied from 16 to 47 years and the duration of amenorrhœa beyond expected menstruation from 3 to 47 days. Out of the 90 recorded cases 30 either were known to be pregnant before treatment began or were later found pregnant on clinical or biological investigation. They were therefore not expected to respond to treatment which in no case caused bleeding to occur.

Technique.—The routine adopted for patients with previously normal or only slightly irregular menstrual histories consisted of one intramuscular injection of 1 mg. of prostigmin on three successive days, this treatment being discontinued if after the first or second injection the menstrual flow was restored. With the exception of two cases which failed to respond, the longest interval between the last injection and the onset of menstruation was about 72 hours. These periods were normal in quantity and duration, and in two cases biopsy proved the flow to be of a truly menstrual character.

TABLE OF RESULTS

Group	Number of cases	Bleeding occurred
1	30	Nil
2	24	82.8 per cent
3	36	94.5 per cent
Control	10	Nil

Group 1: Pregnant cases.

Group 2: Poorly selected cases; 1-mg. doses of prostigmin injected, only occasionally 1 mg.

Group 3: Properly selected cases; 1-mg. doses given from the beginning.

Controls: Out of groups 2 and 3; sterile water injected.

Illustrative case.—A 2-para. Has always had regular periods, and presented herself in March and April with

a delay of three days each time. She was treated with prostigmin. After one injection of 1 mg. on each occasion a normal period started. In August she had a delay of 8 days. Two full courses of prostigmin at an interval of 8 days had no effect. An A-Z. test was returned positive, and later the pregnancy was confirmed clinically.

COMPLICATIONS

A number of patients complained of frequency of micturition and giddiness. One woman with a menstrual delay of 8 days complained, 20 minutes after the second injection of 1 mg., of 'a film before my eyes, strong palpitations, sickness, and a terrific rush of water which came out of my mouth'. She rapidly recovered from the attack without treatment. The action of prostigmin on the salivary secretion may conceivably have been the cause of some of these symptoms. This was the only really unpleasant incident in the series.

CONCLUSIONS

It appears that the age of the patient and the length of the menstrual delay are not decisive points in selecting the cases; some observers have reported successful treatment in patients with a delay up to 52 days. The character of the previous menstrual cycle, which should have been quite regular or have shown only slight variations, is of greater importance. Prostigmin is reliable in its action, as is shown by its success in 94.5 per cent of this series. One wonders whether the two failures may not have responded to a fourth injection or to slightly larger doses. The drug causes some minor discomfort of a transient and not serious character, but it is quite safe and pregnancy is not disturbed.

The type of patient we had to deal with raises the question whether a wait-and-see policy or any other 'psychological treatment' may not have been followed by similar success in a considerable percentage of cases. The injection of sterile water in 10 cases, previous to the proper prostigmin course, gave entirely negative results. Even if it were true that in cases of 'functional amenorrhoea' the period will appear sooner or later with rest, tonics, etc., it should be borne in mind that prolonged amenorrhoea may lead to atrophic changes in the uterine muscle. The results are encouraging, and prostigmin deserves further clinical trial. We would suggest that the drug should be tried in all cases of delayed period except those of endocrine origin and those in which pregnancy has been established. Further clinical work may also reveal interesting effects of prostigmin in cases of dysmenorrhoea.

SUMMARY

Ninety cases of amenorrhoea were treated with prostigmin. From 1 to 3 injections of 1 mg. were given. The results obtained were favourable: in 94.5 per cent of the cases of delayed period not due to pregnancy the menstrual flow was restored. Prostigmin is safe; from its use no serious ill effects were observed. There is no tendency of the drug to interfere with the course of pregnancy. This treatment should be reserved for cases with a previously regular or only slightly irregular menstrual cycle.

The Prophylactic Value of Sulfadiazine

By COLONEL D. M. KUHN, and others
(Abstracted from the *Journal of the American Medical Association*, Vol. CXXIII, 9th October, 1943, p. 335)

SUMMARY

1. SULFADIAZINE was administered prophylactically to more than 15,000 soldiers in residence at two posts

where meningococcic meningitis was particularly prevalent during the spring of 1943. In one instance 3 gm. of drug was given by mouth daily for 3 days; in the other the dose was 2 gm. daily for 2 days.

2. Following the institution of prophylactic therapy the incidence of cerebrospinal fever among the treated individuals fell abruptly. Only 2 cases of the disease occurred during a subsequent period of 8 weeks of observation. At the same time 40 cases were found among 18,800 untreated controls.

3. Meningococcus carrier surveys showed that the administration of sulfadiazine by mouth effectively lowered the carrier rate in the treated group at a time when the incidence of carriers among the untreated controls remained high or actually increased.

4. No serious toxic reactions resulted from the large-scale administration of the drug. The treated men continued their usual daily activities without interruption of the scheduled basic training programme during the period of treatment.

Amputation Under Ice Anaesthesia

By S. M. COHEN, M.A., F.R.C.S.
(From the *Proceedings of the Royal Society of Medicine*, Vol. XXXVII, March 1944, p. 232).

A STUDY of mortality figures of amputations in the aged discloses a surprisingly high figure; for example, 59 per cent in 120 cases at the City Hospital, New York, where the extremes of poor and derelict persons are received. To grasp at any method which gives promise of being able markedly to reduce this mortality in itself seems logical. Within recent years the importance of damping down, by the use of cold, the cell metabolism in the anemic limb or arteriosclerotic leg has become generally recognized. The wider use of 'icing' for the limb with arterial embolus, for 'crushing' injury, in shock, indicated the need for trying out this apparently 'safe painless' procedure. I have used the method on 'poor risks' in 11 cases. The original technique of Allen of New York has been closely followed. A tourniquet is essential. Ice-bags are applied for twenty minutes before the icing starts, to the tourniquet site. After applying the tourniquet the entire limb, including an area 2 inches above the tourniquet, is packed with finely chipped ice and enclosed in rubber sheeting. Two and a half to three hours' icing is required for an amputation through the thigh. The method is not a freezing of the tissues; its purpose merely is to lower the temperature sufficiently to interfere with nerve conduction.

The icing is absolutely painless, none of the patients complain of the cold, and they are completely unaware of the tight tourniquet. Blood pressure and pulse records during the icing stage and during the operation show that there is no shock, no after-pain, and pulse sequently no chest complications. Of the eleven cases, all except one had lower thigh amputations, and subcutaneous cases were over the age of 75; eight of the amputations were for arteriosclerotic gangrene, one for an old septic crushed foot, one for senile tuberculous knee-joint, one for gangrene following an arterial embolus. There were no immediate deaths and complete analgesia was obtained, except in two, who had pain on sciatic nerve section (both cases had knee flexion contractures which interfered with adequate refrigeration of the back of the thigh). There were three late deaths—two were 'institutional' deaths, one followed probably pulmonary embolus and is therefore directly connected with the operation. Delay in wound healing was a definite problem, and is a distinct disadvantage. The method may be described as an interesting innovation and is of definite value in diabetic and arteriosclerotic gangrene. The full text of this paper will be published later in the *Lancet*. (For full references see Allen, F. M., and Crossman, L. W. (1943). *Anesth. and Analges.*, 22, 264.)

Recent Advances in Bacteriological Methods

By J. C. CRUICKSHANK, M.B., Ch.B., D.T.M., Dip Bact.
(From the *British Medical Bulletin*, Vol. I, No. 8, 1943, p. 144)

ALTHOUGH there is a constant flow of contributions to our bacteriological knowledge, the most striking advances follow in the wake of some new development in technique. It is of interest, therefore, to consider some of the more important methods which have been described in recent years. An observer returning to the medical laboratory after interval of a decade would note changes in two principal directions. He would be struck by the efficiency of the modern selective culture media for the isolation of bacteria. Further, he would find that the bacteriologist is no longer content to identify an organism as a particular bacterial species but, in dealing with many important groups, regards it as essential to carry the identification a stage further by determining the subgroup or type to which the strain belongs. These types, to which reference will be made later, are a stable character of the organisms, so that the typing methods make it possible to trace the migrations of a strain and frequently to detect the probable source of an infection or an epidemic.

Each of these lines of advance is well exemplified in the investigation of the intestinal pathogens. Many new culture media have been described for their isolation and, while there is little to choose between the best of these, it is clear that they are so vastly superior to media such as MacConkey or Endo agar that the latter may almost be regarded as obsolete for this purpose. In selectivity, satisfactory differentiation of colonies, and rapidity of growth, Leifson's medium, or some modification such as that of Hynes or S. S. (Salmonella-Shigella) agar, has proved outstanding for the isolation of organisms of the typhoid-paratyphoid, Salmonella, and dysentery groups. These media which contain sodium desoxycholate, inhibit the growth of *Bact. coli* and Gram-positive bacteria. The bismuth-sulphite-iron medium of Wilson and Blair is still held in high regard for the isolation of organisms of the enteric group, especially *Bact. typhosum*. It is routine in most laboratories to culture faeces and urine from suspected enteric cases directly on desoxycholate and bismuth-sulphite media, and also to sow a fairly heavy inoculum into a fluid enrichment medium such as tetrathionate broth, from which, after incubation, subculture is made, again on to one or both of the solid selective media. Extensive experience has shown that by this technique the pathogen will seldom escape detection in infective material.

With a series of faecal specimens from dysentery cases inoculated in parallel on Hynes' medium and on MacConkey agar, twice the number of isolations of Flexner's and Sonne's bacilli were made on the former in acute cases and six times the number in convalescence. A tellurite-iron citrate-neutral red agar, with or without rosolic acid, has also proved valuable for the dysentery group. The data obtained from such investigations have necessitated the revision of previous conceptions in respect to carrier rates, the duration of excretion of the organism in convalescence, and the control of chemotherapy.

In the Salmonella group the pioneer work of antigenic analysis by Kaufmann and Bruce-White has been followed up, and many new Salmonella types have been recognized. In this field, however, the most far-reaching discovery was the demonstration by Felix of the Vi or virulence antigen of the typhoid bacillus. This is a labile antigen, associated with full virulence of the organism, found in freshly isolated strains, but readily lost in subculture. It is reasonable to think that an effective antityphoid vaccine should be prepared from a typhoid strain possessing Vi antigen, and laboratory trials and, more recently, experiences in the field confirm that this is so. As heat and most of the antiseptics usually employed to preserve vaccines cause damage to the Vi antigen, Felix prepared a vaccine which was sterilized and preserved with alcohol. This

vaccine has been shown to be safe and to produce a satisfactory response of Vi antibodies in inoculated subjects. Antityphoid serum for therapeutic use should also contain Vi antibodies. A further development of Felix's work was his discovery that the blood of typhoid carriers almost always contains Vi antibodies; the Vi agglutination test has thus become a valuable means of narrowing the field in the search for carriers and the test is, moreover, independent of intermittency of excretion of typhoid bacilli.

In 1938 and subsequent years, Craigie and Yen who had been working with a bacteriophage which was specific in its lytic action on Vi strains of typhoid bacilli, reported that, by propagation of this phage on individual strains, they were able to produce Vi phages specific in their action on these particular strains. These specific phages could thus be used to identify the strains, and typing of typhoid bacilli became possible. Craigie described 18 types and subtypes to which a number of new ones have now been added. A fresh weapon was placed in the hands of the epidemiologist, and already there have come from Britain and America a number of fascinating accounts of the way in which a strain of certain phage-type responsible for an epidemic or a few scattered cases has been traced back to its ultimate source. The technique of phage-typing is a specialized one usually carried out in a central reference laboratory, but facilities for its performance should be available to all public health investigators.

In the bacteriological diagnosis of diphtheria it is now acknowledged that it is necessary to use a selective medium containing tellurite. The laboratory which relies, as in the past, solely on Löffler's serum is likely to miss some of the acute cases and to fail to detect the diphtheria bacillus in a large number of contacts, carriers and convalescents. The ideal tellurite medium would be easily prepared, would grow typical colonies of all diphtheria strains in 24 hours and would inhibit other organisms. Further, the microscopic morphology of the organisms would be readily recognizable. The perfect medium has not yet been devised, but of the various formulæ which approach it more or less closely, that of Hoyle is one of the most popular. This medium contains blood, lysed by saponin or other means, and is especially successful when prepared with a meat extract base by a method which avoids excessive heating. The good tellurite medium also permits easy identification, by differences in colony form, of the *gravis*, *intermedius* and *mitis* types of diphtheria bacilli, a differentiation confirmed by subculture into certain other media including starch, which is fermented only by the *gravis* type. These types, which all produce the same toxin, were first described by Anderson, Happold, McLeod and Thomson in Leeds, where the *gravis* type was always, and the *intermedius* type almost always, found to be virulent to guinea-pigs. These two types are associated as a rule in man with more severe infections than the *mitis* type, which may, however, also cause severe and even fatal infections. Typing of diphtheria bacilli has frequently assisted in the detection of carriers responsible for outbreaks and has already afforded valuable information concerning cross-infection in hospital wards. Typing data collected over long periods throughout the world promise ultimately to give a better understanding of the epidemiology of diphtheria and the long-term relations of the organism to the human herd.

Hæmolytic streptococcal infections in the past presented many problems to the investigator. Many of these are still unsolved, but the technical advances of the last 15 years have made it possible to distinguish the findings which are significant. Streptococci isolated from swabs or infective material must first be shown to be true β -hæmolytic streptococci by the ability of a young fluid culture to lyse a suspension of horse erythrocytes. Organisms giving a positive soluble hæmolysin test may then be classified into one or other of the serological groups described by Lancefield. This test, performance of which presents no great difficulty, consists in extracting from the organisms by acid, or

by Fuller's formamide method, a carbohydrate substance which gives a precipitation reaction in the presence of the appropriate group antiserum. Thirteen groups designated A to M are recognized and, while certain of the other groups are not without pathogenicity for man, the hæmolytic streptococci which are of major importance in human infections belong to group A. Group A organisms are, however, not infrequently found in the normal throat, and identification must be carried a step further. By means of agglutination tests with absorbed sera, technically rather more difficult than the grouping procedure, Griffith defined 23 types within group A. New types are constantly being recognized, and certain types are found in frequent association with certain forms of infection, so that one may refer, for example, to a 'common scarlet fever type'.

Lancefield and Griffith may be said to have played the same rôle as an earlier bacteriologist of whom it was said that he shook the tree for his followers to pick up the apples. Their methods rapidly led to new discoveries. It was confirmed, as the clinician had already suspected, that the same hæmolytic streptococcus may give rise to various manifestations in a single community. The search for, and isolation of, carriers was put on a more rational basis. New information relating to cross-infections in surgical and fever wards became available. Nowhere was the value of the new techniques more strikingly shown than in the careful investigation into puerperal fever by the workers at Queen Charlotte's Hospital in London. Only by the typing method could it have been proved that endogenous infection, i.e. infection of the placental site by organisms already present in the genital passages at the commencement of labour, is almost negligible as a cause of puerperal fever, and that the important sources of infection are to be found in the attendants or other contacts, or more rarely in the upper respiratory passages of the patient herself.

It was natural to hope that some equally satisfactory classification might be possible in the staphylococcus group. *Staph. aureus* infections are important to the surgeon, and in skin conditions, especially in children, and it is being increasingly recognized that certain strains are responsible for a frequent form of bacterial food poisoning. In view of the ubiquity of staphylococci it is desirable that there should be some means of identifying pathogenic strains and, if possible, of typing them. The coagulase test which depends on the ability of a strain to form a coagulum in human or rabbit plasma, is the most reliable of the suggested methods of identifying potentially pathogenic and toxigenic strains of *Staph. aureus*. Although typing of staphylococci has not so far given such spectacular results as that of streptococci, the method has proved of some value and will probably be developed. It was studied by Cowan who, by observing agglutination of suspensions by absorbed sera on a slide, was able to divide strains into three main types and a number of additional subtypes. In an investigation suggested by the isolation of staphylococci from the inside of surgeon's gloves after operations, he and his colleagues showed that carriage of the organism on the hands was related to chronic carriage of the same type in the nose. Attempts by Fisk to apply phage-susceptibility of staphylococci for purposes of identification are still in an experimental stage.

The present war, like the last one, has provided a stimulus to the study of the organisms of the gas-gangrene group. The best methods of using the existing techniques have been studied and defined. The examination of anaerobic bacteria on a large scale has been hampered by the need of special apparatus, and it is of interest to note the development of methods of growing these organisms in the presence of air. This may be done by adding to fluid media, which must be heated immediately before use, 0.1 to 0.2 per cent of agar and certain reducing substances such as ascorbic or thioglycolic acid. Vigorous growth of anaerobes can also be obtained in ordinary broth or peptone water by the addition of a small strip of sheet-iron. Characteristic changes produced in certain of the iron

media provide additional means of identification.

The overcrowding which occurs stimulates research on airborne infection, a matter of high importance owing to the difficulty of controlling such disease. The sampling of bacteria in the air presents a problem, since the older method of plates of culture media for a prolonged time in the selective capture of the heavy bacteria. This has been overcome by the slit-plate method by Bourdillon, Lidwell and Thomas. A vacuum pump is drawn through a slit by means of a vacuum pump and made to impinge on a rotating plate of culture medium, if necessary, a medium containing gentian violet which will permit the selective growth of streptococci indicative of respiratory pollution. The collection of data from samples thus obtained during short periods under different conditions has put these studies on a new footing and made possible the adequate control of experimental work on aerial disinfection by hypochlorites, hexyl-resorcinol, propylene-glycol and other agents.

The amazing discoveries in the sphere of chemotherapy have been a close concern of the bacteriologist, who has himself not been idle in the search for substances with bactericidal or bacteriostatic action. Penicillin, which may prove, when the problem of production in adequate quantity is solved, to be one of the most valuable of these agents, is the discovery of a bacteriologist, and other substances extracted from bacteria and fungi are constantly being investigated.

The widespread use of the drugs of the sulphonamide group has caused the bacteriologist to modify certain of his methods. He now frequently receives blood or other material for culture containing a sufficiently high concentration of the drug to inhibit growth of the organisms *in vitro*. To counteract this, para-aminobenzoic acid is added to the culture medium; this substance, which is an essential growth factor for many organisms, is utilized by means of an enzyme, the action of which would otherwise be diverted by the chemically similar sulphonamide.

The methods noted above are some of those which are already yielding results of practical importance in the diagnosis and control of disease. The past few years have also seen the appearance of apparatus of great interest to workers in various branches of science which will undoubtedly further our theoretical knowledge of bacteriology and immunology. The Electron microscope which extends resolving power to a present potential limit of about 50 Angstrom units has already given new information concerning the morphology of bacteria and viruses, and the character and thickness of films of antibody on sensitized bacteria. It is probable also that the study of viruses, phages and antibody complexes will be greatly advanced by the use of the new high-speed centrifuges, the largest of which, the Svedberg centrifuge, runs at speeds up to 65,000 revolutions per minute.

A Clinical Evaluation of Some Tests of Liver Function

By G. HIGGINS

J. R. P. O'BRIEN

A. STEWART

and

L. J. WITTS

(Abstracted from the *British Medical Journal*, i, 12th February, 1944, p. 211)

THE subjects studied in this investigation were 100 healthy students and laboratory workers, 71 patients with disease of the liver, and 62 patients suffering from other diseases. Every care was taken to establish the clinical diagnosis beyond doubt.

The laboratory tests in all cases included estimations of the bilirubin, phosphatase, albumin, and globulin in

Reception plasma, and measurement of the hippuric acid excretion and laxulose tolerance.

Analysis of the results indicates that a combination of data of this type has considerable diagnostic and prognostic value.

Changes in the plasma proteins in disease of the liver are of great significance. In cases of hepatitis with jaundice there is a close correlation between the time the jaundice has been present, the changes in the albumin-globulin ratio, and the prognosis. Irreparable liver damage has probably occurred if jaundice persists for more than two months or the plasma albumin falls below 2 g. per cent. In such cases the plasma globulin is usually over 4 g. per cent.

Estimation of the amount of bilirubin, phosphatase, albumin, and globulin in the plasma from a single blood specimen usually provides as much diagnostic and prognostic information as can be obtained from more elaborate tests of liver function.

Full case reports with protocols of the biochemical tests can be obtained from the authors.

Home-made Penicillin : A Warning

(From the *Lancet*, i, 26th February, 1944, p. 284)

In the United States the impression is spreading that the production of penicillin preparations suitable for external application is a simple matter that can be undertaken in laboratories possessing limited facilities, or even in the kitchen. Raper and Coghill, who are working on the production of penicillin for the U.S. Department of Agriculture, think the time has come for a warning. It is, they say, misleading if not actually dangerous to say that *Penicillium notatum* is the green or blue-green mould found on bread, cheese or other foods; it does grow on these things, but so do many other blue-green moulds. There are, in fact, scores of blue-green species in the genus *penicillium* which can be distinguished from *P. notatum* only by painstaking cultivation and microscopical examination in the laboratory. Of a large number of moulds obtained from foodstuffs, fruit, soil and other sources not one in a hundred have been *P. notatum*, and even these often yielded no appreciable quantity of penicillin. Many of the moulds so far studied have been shown to produce substances which are as harmful to animals as they are to bacteria—one has lately been advocated as a rat-poison—and the same is likely to apply to the legion which have not yet been investigated. Moreover, cultures of genuine *P. notatum* are liable to become contaminated with other species or with pathogenic organisms, and this is particularly likely to happen when the mould is grown under 'home-made' conditions. Patients, too, may become sensitive to the mould proteins which are always present in crude preparations, especially when a large raw area, such as a burn, is being treated. The purified preparations of penicillin are protein-free, and each batch is tested for activity, toxicity and sterility. To sum up, Raper and Coghill feel that home-made penicillin can be dangerous. But they recognize the importance of the attempts to evolve a simpler penicillin therapy, and the Minister of Health has also expressed his interest in this work.

The Clinical Significance of the Plasma Vitamin A Level

By H. POPPER, M.D.

and

F. STEIGMANN, M.D.

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXIII, 25th December, 1943, p. 1108)

SUMMARY AND CONCLUSION

THE clinical significance of the plasma vitamin A determination in diseases of the adult is discussed on

the basis of statistically evaluated examinations and on perusal of the literature. Under physiologic conditions and with normal nutrition, the vitamin A level is constant at certain times of the day and on consecutive days. Aberrations of the plasma vitamin A level, therefore, assume significance. In liver disease, the plasma vitamin A level is sharply lowered, often to zero. The reduction parallels the degree of liver damage and not the degree of type of jaundice. In the course of recovery the plasma vitamin A returns to normal or even high levels. The vitamin A determination may help, therefore, in the diagnosis and prognosis of liver disease. The reduction of the vitamin A level in liver disease is due partly to impaired intestinal absorption and partly to disturbed release of vitamin A from the liver, both in turn depending on the degree of liver damage. In infection the plasma vitamin A level is reduced, especially in lobar pneumonia, zero levels being found usually during the toxic stage of the disease. Repeated determinations of the vitamin A level are of prognostic value. The plasma vitamin A level is also lowered in various other conditions (e.g. anaemia, gastro-intestinal carcinoma), especially in severely sick patients. The reduction of the plasma vitamin A level in the latter renders it a non-specific index of the general condition. In kidney disease the vitamin A level is often much increased. Hypovitaminæmia A may rapidly develop and is in this country more commonly caused by processes within the body than by faulty nutrition.

Sulfadiazine in the Treatment of the Common Cold

By R. L. CECIL, M.D.

MAJOR N. PLUMMER

and

W. G. SMILLIE, M.D.

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXIV, 1st January, 1944, p. 8)

1. SEVENTY-two colds in 66 different persons were followed clinically and bacteriologically; 48 received sulfadiazine 3.0 gm. daily by mouth for four days, while 24 served as controls.

2. Following sulfadiazine, the nasopharyngeal flora as observed by serial cultures showed a uniform decrease in total number of organisms and a check in the growth of pathogens.

3. The clinical course of the treated colds showed no striking difference from that of the controls; however, there appeared to be some amelioration of symptoms due to control of secondary bacterial infection.

4. As a result of this study, we are opposed to the routine use of sulfonamides in the treatment of the common cold but would favour their use in a few selected cases as a protection against severe secondary infection.

Amœbic Abscess of Spleen

By J. R. FRANK, F.R.C.S., R.A.M.C.

(From the *British Medical Journal*, i, 1st April, 1944, p. 458)

AMŒBIC abscess of the spleen is very rare, and when it does occur is usually associated with amœbic hepatitis. In this case there was no clinical evidence of liver involvement.

CASE RECORD

On 1st April, 1943, an Indian girl, aged 12, was brought for examination. She gave a history of pain in the left lumbar region of 30 days' duration and swelling in the same region for 21 days. She had no urinary symptoms and passed a normal stool once each day. She had been under observation elsewhere

for 15 days, and during this time had had a temperature ranging between 99°F. and 104°F. Her pulse rate had varied between 90 and 110. Quinine and sulphamidamide had both been given without effect.

The child had obviously lost weight. Her pulse was 110 and temperature 103°F. The heart and respiratory system showed no abnormality. On abdominal examination her spleen was found to extend downwards and forwards to below the level of the umbilicus, and was extremely tender. The liver was neither enlarged nor tender. The hæmoglobin percentage was 60, the red blood count 3,400,000, and the white blood count 13,400—neutrophil polymorphs 80 per cent, lymphocytes 18 per cent, and large mononuclears 2 per cent. The urine showed no abnormality. A provisional diagnosis of amœbic splenitis was made, and a course of emetine, gr. $\frac{1}{2}$ daily for 10 days, was begun.

On the following day, 2nd April, cysts of *Entamoeba histolytica* were found in her stools. On 5th April her temperature reached 103°F. and a fluctuating swelling had developed below the left costal margin over the spleen. From this 40 c.cm. of pus was aspirated. The pus was similar to that from an amœbic abscess of the liver, was sterile on culture, and no organisms were found in smears. No *E. histolytica* were seen in it. After this aspiration her temperature never rose above 98.8°F. On 9th April, 10 c.cm. of typical amœbic pus was aspirated. On 5th May the patient was free from pain, her spleen was not palpable, and she had no disability.

Bacillus Proteus OX19 Agglutinated by the Serum of Pregnant Women

By I. GRATCH

(From the *American Journal of Surgery*, Vol. LX, June 1943, p. 411. As abstracted in *Tropical Diseases Bulletin*, Vol. XLI, March 1944, p. 197)

DURING the preliminary stages of a survey of the incidence of rickettsial diseases in the Philadelphia area it was noticed that the sera of pregnant women agglutinated *Proteus OX19*.

An investigation directed towards this point gave the following results:—

	Sera examined	Positive to OX19	Negative
Men.	412	22	390
Non-pregnant women	295	7	288
Pregnant women . .	505	505	0

A further finding was that all the non-pregnant females who had positive reactions were suffering from carcinoma. So also were two of the males with positive reactions; two other males had been vaccinated with *Proteus vulgaris*; in the remaining 18 no cause could be found for the positive reaction.

The stage of pregnancy at which the reaction becomes positive and the time taken for it to become negative after delivery remain to be discovered. In one case of a 12-year-old girl the reaction was weakly positive at an early stage while the diagnosis was difficult and the Friedmann test was still negative; 12 days later there was agglutination at a titre of 1-1,024.

A rapid simple test was employed in which a drop of serum was mixed with a drop of OX19 suspension on a glass slide. The results were controlled by carrying out a simultaneous standard reaction in 50 pregnant women, and the titre was found to range from 1-256 to 1-1,024.

The implications of the test are discussed; it may prove to be a simple early test for pregnancy, and even for malignant tumours, subject to certain limitations, some of which are already known while others remain to be worked out.

Sulphonamide Allergy

By R. G. PARK, M.B.N.Z., M.R.C.P.

(Abstracted from the *British Medical Journal*, i, 10th June, 1944, p. 781)

THE specificity of the sensitivity in 40 cases allergic to sulphonamide drugs has been investigated.

In 60 per cent the allergy was confined to one sulphonamide drug. In 40 per cent it occurred multiple sulphonamides and to sulphanilic acid.

In about half of the latter allergy was to the sulphonamide radical, $\text{NH}_2\text{C}_6\text{H}_4\text{SO}_2$ —in the other half it was to the amino-phenyl radical, $\text{NH}_2\text{C}_6\text{H}_4$ —reactions also occurring to procaine.

No cases were seen in which the sensitization was to still smaller groups than these.

Water Metabolism in Relation to Hot Weather

By J. M. O'CONNOR, M.D.

(Abstracted from the *Practitioner*, Vol. CLII, June 1944, p. 345)

HEAT PYREXIA

WITH sweating there is a considerable loss of salt. Borchart has shown that the ratio of potassium to sodium in the sweat is greater than in the plasma and in agreement with this he found after an exposure to tropical conditions a definite fall in the potassium concentration of the plasma occurred. The change in sodium concentration in his experiments was comparatively small. If the temperatures in Borchart's observations be graphed against the ratio of sodium to potassium in the serum, it will be found that the correlation, with two explicable exceptions, is remarkably good. High temperatures result in a high ratio. The reverse is probably also true and it seems probable that the disturbance in temperature on exposure to warm conditions is not due altogether to the difficulty in losing heat but also to a disturbance in the ratio of sodium to potassium in the body. The sweating, appearing in the first instance as a regulating response against increase in temperature causes, as a consequence of the greater loss in potassium, the standard temperature towards which the body regulates to rise above the normal level. Observations by Kuno and others support this. When a man is kept under very warm conditions he continues for a time to sweat freely but then quite suddenly the sweating ceases. The correct interpretation of this may be that the standard temperature has passed the actual and the heat dissipating mechanisms are shut down. The individual is then at the onset of heat pyrexia in which contracted skin vessels and the dry skin certify that the temperature which the body endeavours to maintain is at a new high and dangerous level, which will be maintained after the external conditions have ceased to be unfavourable to heat loss.

CONCLUSIONS

The dangers of excessively warm conditions are twofold. The first is the danger of collapse from diminution of the distension of the circulation resulting partly from a dilatation of the circulatory bed and partly from a loss of fluid into the intercellular spaces and through the sweat. The second danger is that an excessive loss of K changing the ratio of Na : K may

cause of hyperpyrexia as a result of which the temperature continues to be maintained at a dangerously high level or to mount still higher even after removal of initial cause. There are, of course, conditions so severe that no device will prevent a fatal rise in temperature, but below this impossible level the danger

of failure of the circulation may be avoided by an adequate supply of sodium chloride and water, and danger of hyperpyrexia by an adequate supply or reserve of potassium. The advantage of the first is confirmed by a wide range of practical experience: the second is, it should be emphasized, speculative.

Reviews

TROPICAL MEDICINE.—By Sir Leonard Rogers, K.C.S.I., C.I.E., LL.D., B.S., F.R.C.P., F.R.C.S., F.R.S., and Sir John W. D. Megaw, K.C.I.E., B.A., M.B. (Hon.), D.Sc. Fifth Edition. With 2 coloured plates and 87 text-figures. J. and A. Churchill Ltd., London, 1944. Pp. x plus 518. Price, 21s.

THE fifth edition of Rogers and Megaw's book is now available, and it has been much more thoroughly revised than the previous editions. Revision has been extensively carried out in the chapters on malaria, kala-azar, trypanosomiasis, typhus fevers, leprosy, and the dietetic diseases. In making these revisions the authors have had in mind the special needs of military medical officers serving in the tropics. The revision has not increased the size of the book; in fact the book is slightly smaller. One of the valuable features of this book is the chapter on general diseases in the tropics. This book is one of the standard books on the subject, and is widely known and used in this country. Both authors had long service in this country and know intimately the tropical diseases of India.

THE MEDICAL ANNUAL, 1944.—Edited by Sir Henry Tidy, K.B.E., and A. Rendle Short, M.D., F.R.C.S. Pp. lxxvi plus 404 plus 71. John Wright and Sons Ltd., Bristol. Price, 25s.

THIS excellent annual appears once again excellently printed and produced for a war-time publication. In the introduction the editors as usual make a brief survey of some of the points of interest discussed in articles and referred to in the book. This year the subjects include infective hepatitis, a special article on which has been written by Colonel W. S. Middleton, consultant physician to the U.S. Army, the triumph of the synthetic drugs over the galenicals, the transmission of poliomyelitis, immunization against diphtheria, the new clinical entity, epidemic nausea and vomiting, fluorosis and dental caries, mass miniature radiography of the chest, malaria, rehabilitation, the new sulphonamides, dyspepsia, peptic ulcer and gastritis, and their common occurrence in the services, the use of gastroscopy. All these subjects are discussed under 'Medicine'. Under 'Surgery' the subjects discussed are numerous and include oedema of the arms following operations on the breast and its surgical relief, the use of the vastus externus muscle for intramuscular injections, the treatment of varicose veins by high ligation and division followed by retrograde injection, the factors contributing to high recovery rate in wounded persons, the rocking method of artificial respiration, the treatment of immersion foot, blast injuries of the abdomen. Under 'Abdominal surgery' are discussed the fall in death rate from appendicitis, the use of the Miller-Abbott tube for intestinal obstruction, surgical measures for the relief of severe hæmatemesis in cirrhosis of the liver, the surgical removal of islet tumours of the pancreas. Under 'Surgery of the central nervous system' are discussed the treatment of war injuries of the brain, the care necessary in applying sulphonamides to the brain, the causation of headaches by reduced intracranial pressure, the headache of tumour, the nature and surgical treatment of sciatica. Under 'Chest surgery' is discussed the surgical removal of growths of the lower end of the oesophagus and also the treatment of traumatic hæmothorax by aspira-

tion. The diagnosis of cancer of the rectum is discussed and the importance of simple digital examination of the rectum is stressed. In other sections the use of stilboestrol with castration in the treatment of carcinoma of the prostate is discussed, as also is sulphonamide anuria and its treatment. Under 'Orthopaedic surgery' acute foot strains in the army are discussed, as also the treatment of fractured femur by mechanical fixation by pins and a special clamp which enables the patient to walk about. Under 'Surgical diseases of children' the conservative treatment of osteomyelitis by mobilization, sulphonamides and intravenous infusion are discussed. Under 'Obstetrics and gynaecology' are discussed hæmolytic diseases of the newborn, toxæmia of pregnancy, and synthetic oestrogens. These and many other matters are discussed in the book; any detailed review is of course quite out of the question. This annual is a very valuable publication.

THE SURGERY OF REPAIR INJURIES AND BURNS.

—By Squadron Leader D. N. Matthews, R.A.F.V.R., M.A., M.D., M.Ch. (Cantab.), F.R.C.S. (Eng.). 1943. Blackwell Scientific Publications Limited, Oxford. Pp. xii plus 386. Illustrated. Price, 45s. Obtainable from Messrs. Macmillan and Company, Limited, London

THIS well-illustrated volume has been offered to the profession when large numbers of general surgeons have to face problems relating to the treatment of facio-maxillary injuries on a scale never encountered in peace time, even by specialists in plastic surgery.

Its usefulness will be most appreciated by the general surgeon who may have to perform a plastic operation when the services of a special unit cannot be secured. In forward areas especially, a knowledge of the basic principles of plastic surgery is of great importance to the surgeon who may have to carry out the preliminary toilet and first-aid repair of a facial wound. By a study of Squadron Leader Matthews' book he will do this with much more sympathy for and understanding of the work that will fall to the plastic surgeon when the patient reaches the base.

Even in the deliberate surgery of peace time, it is better that the general surgeon who operates on carcinoma of the lips, cheek, tongue or jaws should understand something of the methods that will be employed by his plastic colleague at a later stage, and plan his incisions accordingly.

This book provides just enough information, clearly set out to guide the general surgeon in his approach to these problems. The book is divided into four parts. Part I deals with immediate repair in general and covers a vast area, bringing in as it does such subjects as traumatic asphyxia, crush injury of limbs, nerve and tendon suture, and abdominal and chest wounds. The only serious criticism of the book is that this first part goes far outside the scope of the plastic surgeon, and no doubt the general surgeon who reads it will already have familiarized himself with such matters. Part I tries to do too much and therefore does it inadequately.

In parts II, III and IV the writer is on safe ground however, and is making a real contribution to surgical literature. Part II deals with subsequent repair and he describes fully and clearly the methods of dealing with

skin loss. The technique of skin-grafting, the fashioning of local skin flaps, pedicle flaps, approximation flaps and lined flaps is gone into with great detail. The pitfalls encountered in special areas are so well described that the general surgeon can hardly fail to find a method suitable to his needs if faced with a difficult situation. Base length ratios and the principles of delayed flaps are explained and the uses of fascia fat cartilage and bone grafts outlined. While the advice given on these latter procedures is scarcely enough for those who intend to embark on them, it does serve to make clear the possibilities in dealing with extensive loss of subcutaneous tissues.

Part III deals with the special problems of facial repair and serves to warn the general surgeon to 'keep off the grass' so far as subsequent repair is concerned. The methods of reconstructing the nose, the eyelids, the lips, and of fixing the fractured jaw are described with a wealth of detail and illustrated by good line drawings. These chapters will be read by the general surgeon with interest, though they tend to dissuade him from rushing in on an area where angels fear to tread. They will be of great value, however, to house surgeons and assistants in plastic units who are setting out to learn the technique.

The best section in the book is part IV, dealing as it does with burns and rehabilitation. The classification of burns is simplified. The author recognizes two types only—those with complete epithelial loss, and those with partial loss. The conflicting view-points regarding burn toxæmia are well described, and those who find themselves at a loss to know what to make of the many widely differing methods of treatment will find some comfort and help from a careful study of this section. The author discusses the advantages and disadvantages of closed therapy, and recommends treatment by coagulants only where a sterile surface can be obtained and then only in minor domestic burns, body burns not involving the limbs, and in children and highly nervous people who might be adversely affected by daily dressings. Treatment by dyes has a wider range of usefulness than tannic acid, but for all burns of the face, hands, feet and external genitalia, the author recommends the open method. The uses and abuses of the Bunyan-Standard envelope are discussed. Finally, the place of skin-grafting and restoration of function of the burned hand receive the attention they deserve. The book is well written and well illustrated, and can be recommended with confidence as a book of reference to the general surgeon, and as a textbook to those who are taking up plastic work for the first time.

I. M. O.

THE SYMPTOMATIC DIAGNOSIS AND TREATMENT OF GYNÆCOLOGICAL DISORDERS.—By M. M. White, M.D. (Lond.), F.R.C.S. (Eng.), M.R.C.O.G. 1944. H. K. Lewis and Company, Limited, London. Pp. ix plus 229, with 110 illustrations. Price, 16s.

THIS short volume, published by Messrs. H. K. Lewis in the General Practice Series, is intended to help the general practitioner in treating patients with minor gynæcological ailments and in deciding which cases should be referred for specialist treatment. The book is written from the standpoint of symptoms, not diseases, and is easy of reference. Such gynæcological treatments as can be carried out in the consulting room are described in detail and are well illustrated. A section on birth control, on certain distressing antenatal symptoms, and on the application of radiation therapy are included.

The treatment suggested is somewhat dogmatic and is limited to the personal preference of the author, but the medicaments advised have the merits of simplicity and cheapness, and are generally speaking suitable for the hospital out-patient clinic. There is a useful appendix containing a list of proprietary endocrine preparations.

This is a handbook which should be popular in this country.

M. I. N. E.

TEXTBOOK OF SURGICAL TREATMENT INCLUDING OPERATIVE SURGERY.—Edited by C. F. W. Illingworth, M.D., Ch.M., F.R.C.S.E. Second Edition. 1944. E. and S. Livingstone Ltd., Edinburgh. Pp. xii plus 564. Illustrated. Price, 30s.

THE first edition of this book appeared only in January 1943. This second edition appearing after this short interval shows obviously that the book has met with a good reception. As the editor points out in the preface, the main change is in the chapter on the treatment of burns which has been completely rewritten by Mr. Thomas Gibson. The strong point about this book is the view-point from which it is written. As the editor states, the actual operation should be regarded as an incident in the course of treatment in which success may depend to a large extent on ancillary measures of preparation and after-treatment. For senior students, for whom the book is written, operative technique is much less important than a knowledge of surgical treatment in its widest sense. These wider aspects of surgical treatment are well outlined in this book, which we strongly recommend.

COMBINED TEXTBOOK OF OBSTETRICS AND GYNÆCOLOGY FOR STUDENTS AND MEDICAL PRACTITIONERS.—Revised by J. M. Munro Kerr, LL.D., M.D., F.R.F.P. & S. (Glas.), F.R.C.O.G., and others. Fourth Edition. 1944. E. and S. Livingstone Ltd., Edinburgh. Pp. xii plus 1208. 511 illustrations, some in colour and numerous x-ray plates. Price, 42s.

THIS book first appeared over 20 years ago; this is the fourth edition. The whole text has been revised and steps have been taken to bring the book up to date. The alterations are seen mainly in the chapters on analgesia and anaesthesia, on blood transfusion, on the health, nutrition and disorders of the newly born infant, on disorders of function including a section on sterility. The treatment of gonorrhœa with the sulphonamides is discussed in detail. Some coloured illustrations have been introduced into this edition for the first time. This book is intended for medical students, and minute details of surgical technique are wisely omitted.

STERILITY AND IMPAIRED FERTILITY: PATHOGENESIS, DIAGNOSIS AND TREATMENT.—By C. Lane-Roberts, M.S., F.R.C.S., F.R.C.O.G., A. Sharman, M.D., M.R.C.O.G., K. Walker, F.R.C.S., and B. P. Wiesner, D.Sc., Ph.D., F.R.S.E. 1939. Hamish Hamilton Medical Books, London. Pp. xx plus 419. Illustrated. Price, 14s.

THIS is an excellent book. It is written by four specialists, two of them gynæcologists, one a genito-urinary surgeon and the fourth a biologist. It should do much to enlighten and aid the general practitioner and the specialist in the understanding and treatment of the many-sided subject of infertility. It contains an able exposition of the present state of knowledge of the scientific principles underlying the problem, and describes in detail practical methods of investigation and treatment.

Much of the subject-matter will be new to many. Especially interesting is the section on the estimation of male fertility and the relation between low fertility in the male and the tendency to abortion in the female. Recent work has shown that the responsibility of the male in childless marriage does not end with fertilization, and that in cases with this ætiology, treatment with endocrine therapy may be successful.

The importance of the investigation of both partners when faced with the problem of sterility is still too often lost sight of, and few practitioners have equal knowledge of the subject in both the sexes. This book is of great value in bringing together in one volume details of the methods of investigation of both the male and the female.

A book to be strongly recommended.

M. I. N. E.

TEXTBOOK OF MEDICAL TREATMENT.—Edited by D. M. Dunlop, B.A. (Oxon.), M.D., F.R.C.P. (Edin.). Third Edition. 1944. E. and S. Livingstone, Ltd., Edinburgh. Pp. xi plus 1218. Price, 30s.

THIS book published in 1939 is already in its third edition and extensive alterations have been found necessary. A special section on the clinical use of the sulphonamide drugs has been inserted and this prevents the frequent repetition in the different sections in the book of the same information. Several sections of the book have been partly or completely re-written. These sections include those on cerebro-spinal fever, sprue, hæmorrhagic and hæmolytic diseases, compressed air illness, diabetes of pregnancy, and several others. To all the sections new matter has been added. Throughout the book emphasis is laid on the general management of the case. Although drug treatment is very fully discussed, the number of drugs recommended is kept within reasonable limits, but of those that are mentioned full details are given. This is a most useful book for the medical student and the practitioner.

AVIATION MEDICINE.—By Harry G. Armstrong, M.D., F.A.C.P. Second Edition. 1943. Baillière, Tindall and Cox, London. Pp. xiv plus 514. 86 illustrations. Price, 36s.

THIS book now in its second edition was first published in 1939. In the preface it is stated that most of the recent work in this field is classed as confidential and cannot be published till after the war. To this second edition therefore new material has been added but no drastic revision has been attempted. The scope of the book is best indicated by mentioning of the chapter titles: the flight surgeon, pilot selection, examination of the eye, cardiovascular system, ear, nose and throat, general physical examination, neuropsychic examination, care of the flyer, noxious substances in aviation, physical factors in flight, aerial equilibration, orientation and air sickness, acute altitude sickness, anoxia, aeroembolism, speed and acceleration, emotional reactions to flight, etc. These subjects and others are discussed in a most interesting way. This new branch of medicine obviously provides a fascinating field of study and speculation.

ANTENATAL AND POSTNATAL CARE.—By Francis J. Browne, M.D. (Aberd.), D.Sc., F.R.C.S. (Edn.), F.R.C.O.G. Fifth Edition. 1944. J. and A. Churchill Ltd., London. Pp. viii plus 622. 87 illustrations. Price, 24s.

THIS fifth edition has been thoroughly revised. A new chapter on the Rh factor has been included and recent work on diet in pregnancy has also been discussed. The chapters on radiology in obstetrics and on internal pelvimetry have been extensively revised.

MODERN TREATMENT YEAR BOOK, 1944.—Edited by Cecil P. G. Wakeley, C.B., D.Sc., F.R.C.S., F.R.S.E., F.A.C.S., F.R.A.C.S. (Hon.). The Medical Press and Circular, London. Pp. viii plus 301. Price, 16s.

THIS book contains 42 articles by well-known authorities, exactly half the articles being on war medicine and surgery. It is impossible in a short review to make any comment worth while on such a wide range of subjects. All the articles are short and give in small compass an outline of the present position of treatment of the many conditions discussed. This book has been produced every year by the *Medical Press and Circular*, a very lively and stimulating little journal.

A.R.P. MEDICAL MANUAL NO. 3 (INDIA). 'FIRST AID POST AND THE DOCTOR'

THE manual briefly describes the type of work performed in first aid post which have been organized to safeguard the civil population against the effects of air attacks, and is intended for the use of medical

officers and other personnel. It is divided into four parts. Part I deals with the medical organization concerned with the treatment and transport of air raid casualties and describes the functions of the first aid post and of the various services connected with it. Part II gives general information regarding types of missiles, types of injuries and principles of treatment, stress being laid on the fact that 'no air raid wound should be considered trivial or negligible unless proved otherwise by careful and thorough examination'. Part III describes individual injuries or conditions such as shock, hæmorrhage, burns, head injuries and other types of casualties, and their aid post treatment. Part IV consists of six appendices dealing with scale, care and maintenance of equipment, record forms, etc. It is recommended that this manual should be read with the A.R.P. Medical Manual No. 2 (India).

Abstracts from Reports

THE ANNUAL REPORT OF THE BRITISH EMPIRE LEPROSY RELIEF ASSOCIATION, MADRAS PROVINCIAL COUNCIL, FOR THE YEAR 1943-44

THIS report is twenty pages long and discusses many points of interest. The following developments are mentioned: The reorganization of leprosy departments in the General Hospital and the Stanley Hospital, the recognition of leprosy as a special subject in the medical curriculum and the appointment of a lecturer in the subject. The Secretary of the Council, Dr. R. G. Cochrane, has been doing this work in addition to being Chief Medical Officer of the Lady Willingdon Leprosy Sanatorium and Honorary Director of the investigation units working in several parts of Madras. As he himself says progress will not be maintained if the working of these units is largely the responsibility of one individual.

The report mentions the order of the Surgeon-General that District Medical Officers are to admit to hospitals cases of leprosy needing urgent medical or surgical treatment but the report seems to imply some reluctance to carry out the order. The appointment of an Honorary Publicity Secretary to the Madras Council is mentioned and the work so far done is outlined. A comprehensive post-war programme has been placed before Government covering a period of 20 years. 'It can be definitely said that the work of the last decade in the Madras Presidency has helped greatly in formulating an anti-leprosy programme which holds out a reasonable hope of bringing leprosy under control.' The report gives details of the work of the Silver Jubilee Children's Clinic covering epidemiological investigations and clinical investigations; the work of the Rural Investigation Centre, Polambakkam, and the attempts made there to control leprosy by night isolation of the infectious cases is described. The work of the Urban Investigation Centre, Madras, is mentioned including the follow-up of cases and their contacts and the treatment of cases at the Stanley Hospital. A scheme for the systematic examination of every child in the school in Madras city is mentioned. The need for a leprosy hospital in Madras with 500 beds is stressed.

The work of the Children's Leprosy Sanatorium at Ettapur is described. Here 39 children with leprosy are maintained and treated. The work of two special clinics, one at Madura and the other at Cuddalore is described and also the work of a Field Survey Unit. In two village surveys the incidence was over 120 per mille and it is pointed out that closely adjacent villages may show very marked differences in incidence. The clinical, pathological and immunological studies carried out at the Lady Willingdon Leprosy Settlement are described. A study of the Wassermann and Kahn tests in relation to leprosy indicates that frequently leprosy

causes a positive reaction. The work of the leprosy department in the General and Stanley Hospital is outlined, as also the publicity work of Mr. T. N. Jagadisan. During 1943 two post-graduate courses were held. During the year the Public Health Act, 1939, has been modified in such a way as to make anti-leprosy measures more practicable. A memorandum on leprosy work in post-war reconstruction has been submitted to the Government of Madras.

REPORT OF THE SUDAN MEDICAL SERVICE, 1942

This report surveys the health of the Sudan. The following diseases are mentioned as being prevalent in certain areas: relapsing fever, cerebro-spinal fever, schistosomiasis (*haematobium* is reported as increasing but as being relatively mild; *mansoni* is becoming endemic in some areas and in this infection the prognosis is much worse), kala-azar, malaria, sleeping sickness, syphilis, pulmonary and non-pulmonary tuberculosis and malignant disease. The use of rectal swabs in the diagnosis of bacillary dysentery is mentioned.

Correspondence

NATARPHAL (*C. BONDUCELLA*) IN MALARIAL FEVERS

SIR,—Caesalpina jayabo (*C. bonducella*) (Natarphal) was given a clinical trial in the outdoor of the Chittaranjan Hospital, Calcutta, in cases of malarial fever as a substitute for quinine during the epidemic of 1943 when supply of the latter drug fell short of requirement.

Doses used were 15 grains of the dried kernel in powdered form for a dose, three times a day orally. Altogether more than two hundred cases were treated with this drug.

The results of investigation may be summarized as follows:—

(1) In cases of benign tertian and quartan infections temperature was brought under control and fever subsided in 5 to 6 days, and roughly after a total dosage of 250 grains of the powdered kernel orally.

(2) It did not prevent the relapse and in many cases fever recurred after about a week, i.e. after a total dosage of about 300 grains of the drug orally, but intensity of fever during relapse appeared to be milder in respect of temperature and other symptoms.

(3) Malaria parasites were quite evident in blood slides after oral administration of the drug for three days in the above doses.

(4) It has no influence on fever caused by mild attacks of malignant tertian infection in which it was tried.

(5) The drug in the above dosage produced no untoward symptoms except a little gastric irritation in a few cases.

Compressed cinchonæ bark tablets were also used in about 50 cases of malaria fever.

The dose used was 10 grains for a dose thrice daily for 6 days. The result was not better than that with Natarphal.

Conclusion.—Natarphal (*C. bonducella*) appears to possess antipyretic action to some extent in malarial fevers. In crude form it does not appear to have any influence on the malarial parasites. Trial with cinchonæ bark tablets gave practically similar results. It is very difficult to produce proper concentration of active principles in blood by giving drugs in crude form as has been used in these cases. So further investigation is desirable before any conclusion is drawn about its utility.

S. C. LAHIRI, M.D.

56A, CREEK ROW,
CALCUTTA,
14th November, 1944.

'ENTERO-VIOFORM' AND 'VIOFORM'

SIR,—Our clients desire us to draw your attention to an article entitled 'The quality of Indian-made synthetic drugs II' published in volume LXXIX, no. 10 of the *Indian Medical Gazette* at page 469 and in particular to the following:—

1. 'Entero-Vioform' and 'Vioform' are the trade marks in India of the Society of Chemical Industry in Basle (Switzerland) and may only be used to describe products manufactured by the Society of Chemical Industry in Basle or by its associated houses.

2. 'Vioform' is a trade mark used to describe the chemical substance 'iodochlorhydroxyquinoline', whilst 'Entero-Vioform' describes the substance 'iodochlorhydroxyquinoline and sapamine'. That is to say that the products are not identical, as suggested in line 4 of the article.

3. In table I on page 470, products nos. 2, 6 and 7 are described as Entero-Vioform and product no. 4 is described as Vioform, although, according to the article, no 'Ciba' brand powder is available in India. Thus, these products are apparently substances manufactured by other laboratories and, therefore, should not be described with our clients' trade marks.

4. In table II, which is an analysis of the various iodochlorhydroxyquinoline tablets, the footnote states 'Claim in each of the above sample=0.25 g. entero-vioform per tablet'. According to the table of the 16 samples examined only one sample was Entero-Vioform 'Ciba'. This description is misleading especially as these products do not contain Entero-Vioform, i.e. iodochlorhydroxyquinoline and sapamine, but only iodochlorhydroxyquinoline. Therefore, this table is again misleading and liable to cause confusion in the mind of the reader.

MESSRS. CRAWFORD BAYLEY AND CO.
(Solicitors and Notaries Public).

IMPERIAL BANK BUILDINGS,
BANK STREET, BOMBAY,
20th November, 1944.

Service Notes

APPOINTMENTS AND TRANSFERS

LIEUTENANT-COLONEL C. A. BOZMAN resumed charge of his duties as Additional Public Health Commissioner with the Government of India on the forenoon of the 24th October, 1944.

Lieutenant-Colonel F. H. Whyte was appointed Civil Surgeon, New Delhi, with effect from the 30th October, 1944.

The following officers have been appointed as Assistant Inspectors of Hygiene in the Directorate of Inspection, Department of Food, Division III, with effect from the date shown against each:—

Major P. R. Dutt. Dated 22nd November, 1944 (forenoon).

Major C. V. Ramchandani. Dated 28th November, 1944 (forenoon).

Major P. Chandra. Dated 1st December, 1944.

Major A. I. Lakshminarayanan. Dated 2nd December, 1944 (forenoon).

Major K. L. Malhotra. Dated 4th December, 1944 (forenoon).

Major E. G. Montgomery, Civil Surgeon, Jalpaiguri, is appointed as Inspector of Hospitals, Rajshahi Division, with headquarters at Jalpaiguri. Dated 16th December, 1944.

Captain J. H. Caverhill, officiating Resident Medical Officer, Presidency General Hospital, Calcutta, is appointed as Civil Surgeon, Jalpaiguri. Dated 16th December, 1944.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

To be Captains

Fazl-i-Haque. Dated 8th August, 1943.
Kesava Panicker Narayana Panicker. Dated 5th February, 1944.
Keshav Shamrao Dharadhar. Dated 9th August, 1944.
Venkatramier Rajagopalan. Dated 18th October, 1944.
Puthan Veetil Bala Krishna Marar. Dated 20th October, 1944.
Saileswar Chakraborty. Dated 17th September, 1944.
Nazir Ahmed Bashir Ahmad Vahidy. Dated 18th September, 1944.
Jyoti Prakash Mohanty. Dated 20th September, 1944.
Sheik Abdool Majid Sopher. Dated 9th October, 1944.
Karuna Shankar Prem Shankar Dave. Dated 13th October, 1944.
Gopal Anandrao Kumble. Dated 15th October, 1944.
S. A. F. Shamsul Huda. Dated 19th October, 1944.
Syed Sayeeduddin Ahmad. Dated 20th October, 1944.
Virendra Nath. Dated 26th July, 1944.
Mahmoodul Haque Hashmi. Dated 19th August, 1944.

To be Lieutenants

Padam Devraj Naidu. Dated 14th October, 1944.
Frederick Alexander Saldanha. Dated 18th October, 1944.

19th October, 1944

Konsur Narayana Rao Achyutha Rao.
Bidare Venkataramiah Srinivasa Rao.
Basavapatna Sreekantiah Nagaraj.
Kapil Deo Narain Karan. Dated 21st October, 1944.

INDIAN MEDICAL SERVICE—SECONDED TO THE INDIAN ARMY
MEDICAL CORPS
(Emergency Commission)

To be Captain

(WOMEN'S BRANCH)

Miss Kalangi Jessie Balasundaram. Dated 18th October, 1944.

The undermentioned officers of the I.M.S. (E.C.) revert from the I.A.M.C. and are seconded for service in the Indian Air Force:—

Captain K. L. Chopra. Dated 31st October, 1944.
Lieutenant Nawab Khan. Dated 8th July, 1944.
Captain M. S. Muttukunarasami. Dated 3rd July, 1944.
Captain J. R. Kumar. Dated 19th July, 1944.
Captain A. Das Gupta. Dated 11th August, 1944.
Lieutenant Abdul Ghafoor Sheikh. Dated 20th October, 1944.

To be Lieutenant

Vittal Raghavendra Rao. Dated 8th July, 1943.

LEAVE

Major E. H. Lossing, Civil Surgeon, Tippera, is granted leave on average pay for 8 months, with effect from the 18th October, 1944.

PROMOTIONS

Colonel to be Major-General

J. P. Huban, O.B.E., V.H.S. Dated 31st October, 1944.

Major to be Lieutenant-Colonel

B. S. Nat. Dated 20th November, 1944.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Captains to be Majors

A. E. Stevens. Dated 12th October, 1944.
S. Rodrigues. Dated 15th October, 1944.
K. L. Datta. Dated 1st November, 1944.
P. A. Mathew. Dated 2nd November, 1944.
L. S. Nathan. Dated 15th November, 1944.

Lieutenants to be Captains

V. R. Rao. Dated 20th November, 1943.
W. I. White. Dated 1st July, 1944.

RELINQUISHMENTS AND RESIGNATIONS

The following relinquishments and resignations are permitted.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

Captain Authimbolan Sivabooshanam, on grounds of ill health, 20th November, 1944, and is granted the honorary rank of Captain.

Captain Ramchandran Narayanan, on grounds of ill health, 8th December, 1944, and is granted the honorary rank of Captain.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

Captain Gopal Ganesh Sahasrabudhe. Dated 28th August, 1944.

Captain (Mrs.) D. D'Souza (née Pacheco). Dated 21st October, 1944.

Captain Faqir Mohammad Khan. Dated 20th October, 1944.

Captain Mohd. Abdul Rahman Khan. Dated 18th November, 1944.

Publishers' Notice

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Communications for the Publishers relating to Subscriptions and Advertisements should be addressed to THE PUBLISHERS, *The Indian Medical Gazette*, P. O. Box No. 54, Calcutta.

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The Editors of *The Indian Medical Gazette* cannot advise correspondents with regard to prescriptions, diagnosis, etc., nor can they recommend individual practitioners by name, as any such action would constitute a breach of professional etiquette.

Original Articles

CONTROL OF SEPSIS IN WAR WOUNDS BY PRE-SURGICAL TREATMENT

(PRELIMINARY REPORT)

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EXAMINATION of case records of soldiers dying as a result of war wounds shows that when death occurs more than seven days after wounding, it is generally due to sepsis. The rôle of sepsis in producing prolonged invalidism is even more important, since delayed healing of a soft tissue wound with the attendant troubles of fibrosis and stiff joints is invariably due to infection. Prolonged disability in the case of compound fracture or a retained foreign body is generally due to the same cause.

The main field for improvement in results of war-time surgery thus lies in the advance of treatment of sepsis. Both in this war and in the last, research and clinical investigations into methods of treatment have been actively pursued. Prevention has received less attention, and current surgical teaching implies that, unless excision can be performed within six to eight hours of wounding, sepsis is unavoidable. A consideration of the conditions which obtain at the moment when war wound is infected demonstrates that in many cases this is not so. Although there are published statements to the contrary, it is believed that wounds caused by bullets or fragments of high explosive are sterile at the moment of their infliction, since both bullets and shell fragments are heated to the point of sterility. It has been observed that if the latter are travelling too slowly to penetrate the skin, they may adhere to it and cause a burn. Clothing worn in tropical climates generally tears cleanly when perforated, and it is exceptional to find clothing buried in the wound. The difficulty in treating these wounds lies in the fact that, although sterile, they are extremely vulnerable to infection because they contain quantities of blood clot and a variable amount of dead and devitalized tissues. This difficulty is met by wound excision and subsequent care in hospital surroundings if the patient can be brought under care of an expert surgeon working under hospital conditions within the eight hours' period. Statistics show that these conditions do not and never have obtained widely in military surgery in the field, and the problem here is to elaborate a technique which will protect fresh wounds from super-added infection

during the period which elapses before hospital conditions are reached.

Basis of investigation

With a view to evolving a suitable technique, the following four objectives were defined:—

(1) *Elimination of the risk of infection from surrounding skin.*—The risk of serious infection from skin is high in jungle warfare conditions. This is exemplified by the frequency with which minor scratches and abrasions develop into large jungle sores. Early and thorough preparation of the skin surrounding wounds is essential.

(2) *Elimination of the risk of cross infection.*—Cross infection may occur either by the hands or instruments of attendants, or indirectly by contact between the wound and such articles as blankets and stretchers. It can be avoided by using a 'no touch' technique, by covering the wound efficiently at the first dressing, and by keeping the original dressing in place until conditions are reached which permit redressing with full aseptic precautions.

(3) *Bacteriostasis in dressings covering the wound.*—Dressings soaked in blood and wound discharge form an excellent culture medium. Impregnation of dressings with sulphanilamide was proposed with a view to inhibiting such bacterial activity.

(4) *Alteration of conditions in the wound cavity so that it no longer forms a good medium for the growth of organisms.*—The presence of a sufficient concentration of one of the sulphonamides in a wound cavity renders it a less favourable field for bacterial activity. Local application was selected in preference to oral administration because the blood clot and dead tissue which it is desired to influence are not accessible to drugs carried by the blood stream.

Experimental work

No experimental work has been undertaken in connection with methods of skin preparation or the mechanism of cross infection.

Infection of wounds by skin-borne organisms

It was considered that a dressing which is itself a good culture medium might facilitate the spread of infection from the surrounding skin to wound, and this danger might be partially averted by using bacteriostatic dressings. This question was, therefore, investigated experimentally by (i) studying the bacteriostatic action of sulphanilamide-impregnated pads and (ii) treating experimental wounds in animals by these medicated pads.

The pads were prepared by soaking sterile cotton wool enclosed in a single layer of gauze, in a saturated solution of sulphanilamide and allowing to dry. An approximate estimation of the sulphanilamide content of such pads showed that a pad weighing 20 grammes contained about 2 grammes of sulphanilamide.

(i) *Bacteriostatic action of sulphanilamide pads.*—Several sulphanilamide pads were soaked with 5 c.cm. of dog's blood and smeared with

0.5 c.cm. of thick saline suspension of organisms immediately afterwards. The organisms used were the *B. hæmolytic. streptococcus*, *Staphylococcus aureus* and *B. pyocyaneus*. Control pads (without sulphanilamide) of the same weight were treated similarly. Each pad was enclosed in a separate Petri dish, and put in a glass container with a layer of water underneath. The pads were thus kept in a humid atmosphere and incubated at room (25 to 27°C.) and body temperatures for 4 days. It was found that at the end of this period, the medicated pads were red in appearance and free from offensive smell, while the control pads were dark in colour and intensely offensive. The medicated pads were tested for the presence of organisms and the appropriate organisms could be recovered from them. The action of sulphanilamide was, therefore, found to be purely bacteriostatic.

(ii) *Treatment of wounds with sulphanilamide pads.*—Superficial wounds were produced in the shaved skin of rabbits by several 'criss-cross' incisions. The surrounding healthy skin was then smeared with a saline suspension of *Staphylococcus aureus*. The wounds were then treated by (a) dressing with a medicated pad without any other application, (b) similarly dressing with a medicated pad after application of sulphathiazole paste (*vide infra*). Controls were made by dressing wounds with sterile non-medicated pads.

It was found that combined treatment with paste and pad prevented the surrounding infection from travelling to the wound, and thus promoted healing. The medicated pads alone reduced the degree of infection in the wounds, and evidence of infection appeared on the third day. In wounds dressed with control pads, evidence of infection appeared within 24 hours, and the degree of infection was widespread.

These experiments, therefore, show that impregnation of dressings with sulphanilamide exerts a marked bacteriostatic effect and that infection travels less readily from the surrounding skin to a wound when a bacteriostatic dressing is used. By combination of sulphathiazole paste and bacteriostatic dressings such spread may be prevented altogether.

Sulphonamide preparations for local application to wounds

Clinical observations by one of us (A. J. G.) had suggested that an emulsion containing 30 per cent sulphanilamide in a cod-liver oil base was suitable for the purpose. After preliminary experiments, a 'water in oil' emulsion containing sulphanilamide and cod-liver oil was selected for trial (sulphanilamide 40, calcium oleate 2, bees wax 3, cod-liver oil 60, water 40). Some observations were also made with a similar paste containing about 10 per cent of sulphathiazole.

Experiments were performed with three objects in view: (a) to estimate the bactericidal and

bacteriostatic powers of the emulsion in recent wounds; (b) to estimate the extent of tissue damage which the emulsion is capable of producing under various conditions of application; and (c) to estimate the period over which sulphanilamide continues to be absorbed into the blood stream after local application of the emulsion.

(a) *Bacteriostatic powers of cod-liver oil emulsion.*—The effect of local application of various sulphonamide preparations in reducing mortality after experimental infections by a 'pion' strain of streptococcus has been reported by Hawking (1942). In these experiments the infection was very heavy (estimated at 10,000 m.l.d.). Results show that 'oil in water' emulsions and 'oil' preparations reduce the mortality by 50 per cent and 70 per cent respectively, even under such conditions. Experiments on these lines were not repeated, as our concern was rather to estimate the effect of emulsions on milder infections such as are commonly responsible for prolonged suppuration.

In our experiments, open wounds were produced in dogs by incising the skin over the thigh muscles and damaging the muscles by a few cuts. The paste was applied by squeezing a collapsible tube containing the required paste either directly or through a rubber tube. The skin over the wound was sutured loosely. As a rule, a considerable portion of the applied paste came out while suturing the skin or soon afterwards.

To determine the effect of local application of the paste on infected wounds, 0.5 c.cm. of a saline suspension of *Staphylococcus aureus* (containing about 1,000 million organisms) was applied to damaged thigh muscles in open wounds on both sides of a dog. One side was treated by local application of the sulphathiazole paste while the other was left untreated. By the end of the fourth day the treated wound appeared quite clean, while the untreated one showed pockets of pus. Histological examination of the sites of lesion showed necrotic changes in the muscles around the pockets of pus of the untreated wound, while on the treated side the reaction was considerably less in severity.

These experiments show that sulphathiazole paste is capable of controlling a fairly heavy infection of *Staphylococcus aureus* in dogs.

(b) *Tissue damage produced by cod-liver oil emulsions.*—Hawking (1943) has investigated this subject also, and has summarized previous work. This publication and others by the same author give a full account of the changes produced by cod-liver oil when it is injected intramuscularly or intraperitoneally, and also when it is introduced into a wound which is subsequently sutured. These conditions are not comparable with those which exist when cod-liver oil paste is used for the early treatment of war wounds, as such wounds are never sutured.

A considerable proportion of the oil itself is discharged from the wound cavity within the first few hours, and tissue fluids which are produced by local reaction are free to escape.

Experiments were, therefore, undertaken to compare the change induced in open and closed wounds. The open wounds were made as described before. The closed wounds were obtained by suturing the muscle layers and closely suturing the skin so that no paste could escape. Some experiments were also made by injecting the paste into the thigh muscles by a syringe through a large-bore needle introduced through the skin. No attempt was made in these experiments to damage the muscles artificially. To introduce the paste into serous cavities, suitable syringes and large-bore needles were employed. In most of these experiments, sulphanilamide paste was used and the experiments made on dogs.

Closed wounds.—To study the effect of local application of the paste in closed wounds, about 4 c.cm. of the paste was allowed to remain in contact with the thigh muscles for a period varying from 3 days to 4 weeks. At the end of the period the animal was killed and the site of lesion examined. The following is a brief summary of the findings:—

During the first week there is a considerable reaction in the muscle where the paste is applied. Up to the fifth day the emulsion could be seen at the site and oozed out as soon as the muscles were incised. There was swelling of the muscles and oedema was present. Histologically marked changes were seen. Patchy necrosis was observed and between muscle fibres inflammatory exudate of polymorphonuclear leucocytes and red cells was seen. Some muscle bundles showed loss of striation. This reaction subsided during the second week and at the end of this week the acute reaction was seen to be reprogressing and giant cells were observed. Fibrotic changes began to appear and young fibrous tissue could be seen invading the muscular tissue. This process continued during the third week. During this period the muscles appeared pale and rough to the naked eye. Histologically vascular reactions had disappeared. At the end of the fourth week healing had well advanced.

Open wounds.—The course of events in the open wound was somewhat different.

The very marked reaction seen in closed wounds during the first week was not seen. There was vascular reaction and some oedema of muscles but the degree of reaction was considerably less as compared with that in closed wounds. By the end of the second week fibrosis in the cut muscles had progressed and by the end of the third week it was well advanced. No necrosis could be observed at any stage.

The experiments described above were concerned with the thigh muscles of dogs. A few experiments were also made by applying the paste to the *rectus abdominis* muscles of these animals, and it was observed that although reactions similar to those described above in the case of thigh muscles were observed, the degree of necrosis in closed wounds was considerably less. It is suggested that this difference may be due to the difference in tension of these muscles.

Peritoneum.—The effects of introduction of sulphanilamide paste into the peritoneal cavity

of dogs were similarly studied by killing the animals at weekly intervals. The quantity injected varied between 1 and 2 c.cm. per kg. The findings may be summarized as follows:—

Within the first week there was considerable exudation of fluid into the peritoneal cavity. The physical characters of the peritoneal fluid were like those of a thin oily emulsion. Microscopic examination of the cellular elements of the peritoneal fluid showed that both monocytes and polymorphonuclear leucocytes were present. When the animal was killed after 13 days there was no exudate seen, but considerable adhesions had taken place. The loops of small intestines had adhered to each other and omentum had adhered to the anterior abdominal wall. It was interesting to note, however, that during the two weeks following an intraperitoneal injection of the sulphanilamide paste, the animals did not show any evidence of intestinal paralysis. A similar experiment was repeated in rabbits, and it was found that an isolated loop of intestine removed 48 hours after intraperitoneal injection of the paste and suspended in a Dales bath in Ringer solution, showed normal movements and reacted to acetylcholine and adrenaline normally.

Knee joint.—A small quantity of the paste (0.5 to 1 c.cm.) introduced into the knee joint produced a swelling of the joint and immobilization of the knee during the first week. The swelling subsided during the second week but was still noticeable at the end of second week. An examination of the joint at this stage showed that a brownish stained fluid was present in the joint, especially in the subcondylar bursa. Microscopic examination of the fluid showed presence of monocytes and a few polymorphonuclear leucocytes. Vascular reaction was not noticeable. At the end of the third week, the swelling had completely subsided. The animal could move its joint freely and there was apparently no pain on movement. On opening the joint, there was complete absence of any inflammatory change and the only evidence of the injection of the paste was the presence of a slight brownish pigment. There was no fluid in the joint or in the bursa and no evidence of any resolving inflammation. The surfaces of the opposing bones, however, appeared somewhat less shiny than those of the bones of the opposite normal joint.

Pellicle formation.—In most of the experiments where the paste was applied to the muscles, a thin brownish film was formed over the surface of the muscles. The presence of this film could be detected up to the end of the second week, but the film was absent after the end of the third week. Microscopically the film showed several kinds of cell including polymorphonuclear leucocytes enveloped in a mass of debris. In open wounds, this film possibly forms a covering under which healing proceeds smoothly. It is confirmed that cod-liver oil emulsions produce the changes described by Hawking (*loc. cit.*), but in open wounds these changes are of a less severe nature. The formation of a covering here described as pellicle is seen, but this pellicle disappears within three weeks and does not constitute an obstacle to healing by granulation. Muscle oedema always occurs, but

necrosis appears to be a product of tension as it is absent in open wounds and slight in open tissue spaces. The results of intraperitoneal injections confirm the view that the emulsions should not be introduced into closed tissue spaces. The limited experimental evidence at our disposal suggests that joints are an exception to this rule. There is some clinical support for this suggestion.

(c) *Evidence of continued absorption after treatment of wounds with cod-liver oil sulphanilamide emulsions.*—It must be emphasized that blood and urine concentrations do not give an accurate picture of the effect of local application on dead tissue in blood clot. Hawking's (1941) work shows that by diffusion of sulphanilamide through a layer of dead tissue 2 to 3 mm. thick, a concentration of 26 mg. per 100 ml. was attained in 24 hours. The concentration in living tissue at the same distance from the deposit did not differ significantly from that in the general circulation, and fell to 13.4 mg. per 100 ml. in 24 hours.

We have compared the relative absorption of 'water in oil' and 'oil in water' emulsions, and in conformity with the findings of other workers, our results also show that the absorption of sulphonamides from a 'water in oil' emulsion is less rapid. In our experiments on dogs dressed with sulphanilamide emulsion, it was found that the concentrations of the free drug in the blood in 4, 24 and 48 hours were of the order of 2.2, 1.3 and 0.65 mg. per cent (average of 4 experiments) and after 96 hours only traces of the drug could be detected in the blood. In the muscles themselves, however, the drug could be detected after 144 hours.

Absorption of a 'water in oil' emulsion during the first three days appears to be approximately in the ratio of 4:2:1. Hawking reported a similar ratio in urinary excretion for the first two days after application of an 'oil in water' emulsion. The ratios reported for absorption of sulphanilamide powder or purely aqueous solutions is of the order of 20:1:0. The emulsion tested is, therefore, suitable if continued absorption over a period of 2 to 3 days is required. Clinical trials reported below also show the same result.

Clinical trials

Preliminary trials of wound treatment with sulphanilamide cod-liver oil paste were made in hospital conditions. A cod-liver oil emulsion was chosen because it mixes readily with blood and tissue fluids, and spreads rapidly through wound cavities. At body temperature the paste used is a thick oily fluid and there is no tendency for it to 'cake' and prevent escape of fluids from the depths of wounds. Dressings applied to wound surfaces which have been treated with this emulsion do not adhere, and can be removed without damaging granulations. It is possible that sulphathiazole is a more effective agent than sulphanilamide, though it

diffuses much less readily. The choice has so far been limited by availability, and in the clinical experiments detailed below, sulphanilamide emulsion has been used.

During the preliminary hospital trials, few opportunities arose for observing effects of paste on fresh accidental wounds, as conditions were generally suitable for early excision. Sulphanilamide paste was used as a post-operative dressing in a number of deliberate operations, and the urine examinations showed that excretion of sulphanilamide started within a few hours and persisted at a level of 40 to 60 mg. per cent for 48 hours, falling in the next 24 hours to 20 to 30 mg. per cent. The original dressings were left undisturbed for ten days, and at the first dressing clean granulations were generally found. On one occasion the paste was introduced freely at operation into a wound which led by a small entry into the fascial space of the calf. Severe pain resulted, and sections obtained from the muscle surrounding the track showed aseptic necrosis. This finding corresponds with experimental evidence regarding the part played by tension in causing necrosis. No other untoward results were observed.

Trials in conditions of active warfare have, so far, been on a very limited scale. The technique used has been as follows: soft tissue wounds occurring in areas where surgical facilities are not available were treated by thorough skin preparation followed by injection of sulphanilamide paste delivered from a collapsible metal tube through a sterile rubber nozzle. Wounds were then covered by a special dressing composed of a sulphanilamide-impregnated pad carried on an adhesive bandage. By means of the adhesive bandage wounds were sealed off completely from external contacts.

Five cases which were dressed in this manner were evacuated to base hospitals without further treatment. The original dressings were removed with strict aseptic precautions at a period of 8 to 10 days from wounding. All wounds appeared clean and healthy. In three of them, wound cultures were sterile, one showed a growth of *Staphylococcus albus* from the exit wound only, and in one the result of culture is not known. The cases included two compound fractures and one perforating wound of the knee joint.

Ten wounds treated by orthodox surgical methods were cultured in the same area at the same period after wounding. Nine were described as 'heavily infected' and one showed an abscess which proved to be sterile on culture.

Further clinical trials are in progress.

Summary

An account is given of the indications for adoption of a specialized early treatment of war wounds. Experimental clinical evidence is quoted bearing on the use of bacteriostatic dressings and cod-liver oil sulphonamide emulsions.

Laboratory experiments described in this article were performed at the Haffkine Institute,

Bombay, by the courtesy of its Director, Lieut.-Colonel S. S. Sokhey, I.M.S. Sulphona-mide pastes for use in extensive clinical trials which are now proceeding were manufactured in the laboratories of the Haffkine Institute.

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INTRADIPLOIC EPIDERMOID OF THE SKULL

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Definition

An epidermoid cyst may be defined as a cyst arising from ectodermal cell-rests, and in particular from epidermal primordia. In the literature, varieties of cysts from dermoids, both sequestration and implantation types to cholesteatomas, have been included under the heading of epidermoids. Some authors have included wens or sebaceous cysts in the classification of epidermoids. In a simple dermoid, epidermis, derma and dermal glands appear in the form of a cyst. In the true epidermoid, however, definite dermal structures are wanting.

Epidermoids may be traumatic in origin, but congenital epidermoids may also result due to misplacements of the epithelium.

Incidence

Epidermoids are rare formations which occur most frequently in and about the nervous system, particularly in its cranial portion. They have been called tumor perles, cholesteatomas, perlgeschwulst, and may arise beneath the scalp, within the diploe, between the bones and the dura mater, beneath the arachnoid membrane, or within the ventricles.

Epidermoid cysts arising in the diploe of the bones of the skull are rare. Up to 1939 only 16 cases had been reported in the literature.

Mode of formation

It is now commonly accepted that these tumours arise from ectodermal rests—a hypothesis advanced by Remak in 1854. Such epithelial 'anlagen' deposited between two ectodermal structures, skin and brain, surrounded by mesodermal tissues, form epidural, intradiploic and epicranial epidermoids.

Embryologically it is easy to see how ectodermal cell-rests may become enclosed within the tables of the calvarial bones; both skin and brain arise originally in the same ectodermal cell plate, and are later separated by the ingrowth of mesodermal elements from the lateral cell mass.

On account of the simple epidermal lining, without the dermal elements, Herschl called them epidermoid cysts. It is probable that deep epitheliomas of the skin arise from such cysts.

These epidermoids arising in the diploe of the skull are deep to the pericranium. The ordinary dermoid with its dermal element is superficial to the pericranium.

Case report

The patient was a girl, aged six years. The parents noticed, some time after birth, a small swelling in the head. Labour was normal and the child healthy. The swelling gradually increased in size, but more rapidly during the last year. The girl was brought for advice as the swelling was increasing in size, and was causing pain and difficulty while combing the hair. The swelling was otherwise painless.

The child is a healthy girl. There is a swelling in the anterior part of the scalp in the middle line, 6 cm. above the bridge of the nose. The swelling is oval, 2.5 cm. long antero-posteriorly, 1.5 cm. transversely, and bulging 0.5 cm. above the general surface. Fluctuation is present, and the hair growing over the bulge does not differ from the hair in the surrounding area. There is no pulsation in the swelling.

The bone round the swelling is slightly elevated and margins of the bone are smooth. The deficiency in the bone is about 1.5 cm. in diameter. The tumour appears to be immobile inside the bony defect (see figure 2).

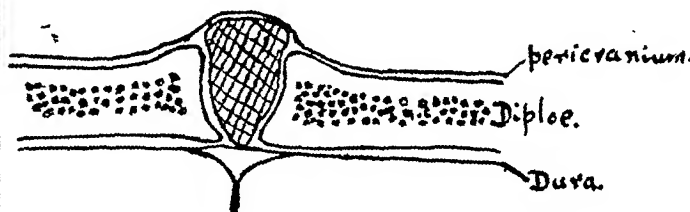


Fig. 2.—Diagrammatic sketch showing the relation of tumour to the surrounding parts.

A roentgenogram taken on 2nd October, 1943, shows a circumscribed deficiency of both the outer and inner tables of the skull (see figure 1, plate IV). The margins of the bony defect are smooth, and there is no evidence of either rarefaction or sclerosis.

Operation.—The patient was operated on under open chloroform narcosis. The cyst which was smooth, was lying deep to the scalp and pericranium. It was separated from the margins of the bone defect without much difficulty, but there was some difficulty from bands of fibrous tissue running from the under-surface of the tumour to the wall of the superior longitudinal sinus, which was left exposed on the removal of the cyst. The margin of the defect in the bone was smooth and shelving, and no diploe was visible. The wound was closed in layers, and convalescence was uneventful.

The cyst was uniform and 1.5 cm. in diameter. No dermal elements were seen in the cyst.

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GNATHOSTOME INFECTION OF THE EYE

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FULL-GROWN adults or immature worms (larvæ) of the genus *Gnathostoma* (Nematoda) have been recorded in man since 1889, and up to 1934, twenty-one cases were published including the two cases from Bengal reported by Maplestone (1929) and by Datta and Maplestone (1930). These twenty-one cases have been listed by Prommas and Daengsvang (1934) in this journal. The third case from Bengal was reported by Maplestone (1932), and in the last ten years, three more cases of human gnathostomiasis have been recorded—two from Bengal by Maplestone and Bhaduri (1937), and Maplestone and Rao (1939), and one from Siam by Daengsvang (1939).

No further case report appears to have been published since 1939; the present case constitutes, therefore, the sixth one from Bengal, and incidentally the first one in which the worm has been found in the eye. It is also interesting that Bengal is the only province in India, in which human gnathostomiasis has been found to occur up till now.

In the previous cases, the worms were found in various places—cutaneous nodes, superficial tumours, breast abscesses; in three instances they were coughed out along with blood; in one instance, the worm escaped from the inner side of the cheek. In the second case from Bengal (Datta and Maplestone, 1930), it was found in the mastoid region, while in the third case (Maplestone, 1932) it escaped from the right eyebrow causing severe inflammation of the neighbouring parts. In one instance (Daengsvang, 1939), a full-grown worm was found in an abdominal tumour which caused symptoms of intestinal obstruction, and the tumour was removed by operation.

In the case we report here, the worm caused severe injury to the eye and would certainly have caused blindness but for prompt surgical interference.

Case report

The patient, a Bengalee Hindu male, age 26, is a railway clerk, living in Calcutta. He had been to his native district in Pabna about a year and a half previously, but he had never been out of Bengal. In Pabna, he had bathed in a tank; he had never eaten raw or dried fish. On 25th May, 1944, he felt a dull aching pain on the left side of his nose. The pain gradually extended up to the left frontal region, and on the next day, a swelling appeared on the left cheek and extended up to the left lower eyelid. Gradually the swelling spread up to the roots of the hair and the patient could not open his left eye. He also had a low type of fever.

On 5th June, 1944, he presented himself at the out-patient department of the Eye Infirmary, Medical College Hospitals, when Captain K. Sen examined him and found signs of orbital cellulitis; vision was normal. Two days later, the cellulitis improved but the vision dropped down to recognition of hand movements only, and there were hæmorrhages in the retina and in the vitreous. He was admitted in the hospital on 8th June, 1944. Three days later, he developed severe iritis with small grey nodules on the iris. After a week the nodules disappeared leaving grey depressions on the iris. Iritis set in again and a large grey nodule and a pigmented nodule appeared on the iris. Both the nodules disappeared, but another pigmented nodule appeared which was seen to move on 12th July, 1944. The next day, definite wavy movements were seen and the worm was removed by operation from the angle of the anterior chamber on 15th July, 1944.

After the operation, the eye condition settled down completely within a very short time.

The parasite

The worm is slightly shrunken, with bits of iris tissue adhering to it (figure 1, plate IV). It measures 3.5 mm. in length and 0.41 mm. in greatest diameter at about the middle of the worm; the head-bulb is 0.116 mm. in length and 0.25 mm. in breadth. Two lateral crescentic lips, each with two papillæ, are present. On the internal surface of the lips three lobes are visible. There are four rows of spines, about 40 in each row, on the head-bulb. The spines have a sharp point projecting through the cuticle, but they have broad roots of varying shapes. In a few spines the roots are notched (figure 2). The cuticle of the body has raised transverse ridges and on the ridges there are spines with simple sharp points. These spines are seen up to the extreme posterior end of the worm. The spines become gradually smaller in size from before backwards so that they appear as simple dots near the posterior extremity. Four cervical sacs are present in the oesophageal region. No genitalia were seen.

The parasite resembles closely that found by Maplestone (1929), but the spines on the head-bulb in our specimen appear to be less developed. Probably this specimen is less mature than that of Maplestone but otherwise the two worms look very much alike. It does not seem that the worm is an immature *G. spinigerum*, because the spines extend almost to the hind end, nor does it seem to be *G. hispidum* because the head spines are not simple structures. We are inclined to believe that this specimen belongs to the same species as that of the worm described by Maplestone (1929), as a new species.

Discussion

In the life-cycle studies of *G. spinigerum* by Prommas and Daengsvang (1933, 1936, 1937), it has been experimentally shown that the eggs of *G. spinigerum* passed by cats hatch in water, and the larvæ enter cyclops. In the cyclops the larva grows and a definite head-bulb with a pair of lips and four transverse rows of spines on the head-bulb with minute

spines on the body appear. Four cervical sacs in the oesophageal region are formed also, and the alimentary system is fully formed. There is no further development of the larva until the infected cyclop is swallowed by fish. In the fish, the larva grows and the spines become well developed but the sex organs do not appear, and it ultimately becomes enclosed in a cyst wall. Non-encysted full-grown larvæ were fed to three cats; in two, typical adults developed in the usual location, i.e. in nodules in the stomach-wall. No experiments were done by feeding cats with encysted larvæ in the fish.

Cats and dogs are the natural definitive hosts of the adult *G. spinigerum*. Another species, *G. hispidum*, is found in the pig but its life history is yet unknown.

The exact way man acquires the infection is still undermined. But from the above life-history studies it is conceivable that the larvæ enter man either through swallowing the infected cyclops with raw water or through eating uncooked infected fish.

It is an interesting fact that in the reported cases from man, both larvæ and adult worms have been found. Man, therefore, appears to be an accidental definitive host like the natural hosts, cats and dogs. The larvæ found in man resemble in their development those in the experimental cyclops and fish. No adult worm has been found in fish so far; man must therefore get the larvæ from either cyclops or fish, if there is no other intermediate host.

It is quite possible that the larvæ may be swallowed by man with cyclops in raw drinking water, but in the six cases found in Bengal fish appears to be an unlikely source as it is always cooked before eating. The fate of the larvæ in dried fish is of course unknown, but dried fish is not eaten raw by the majority of people in Bengal. In the cases in which adult worms have been found, we do not know at what stage the worm entered man, whether as larvæ or as adult; there is no proof yet that the larvæ acquired by man grow to adults—and therefore in cases in which adult worms

have been found, the source of the infection remains an open question. It seems to us that the life history of the worm in Bengal requires investigation.

In whatever way the parasite enters man, it apparently finds the host unsuitable and it migrates in the tissues. During the course of this travel in the body, the worm causes migratory swellings and has caused abscesses in many cases. In the second case reported from Bengal (Datta and Maplestone, 1930), the signs simulated mastoiditis and in the third case (Maplestone, 1932) the worm produced

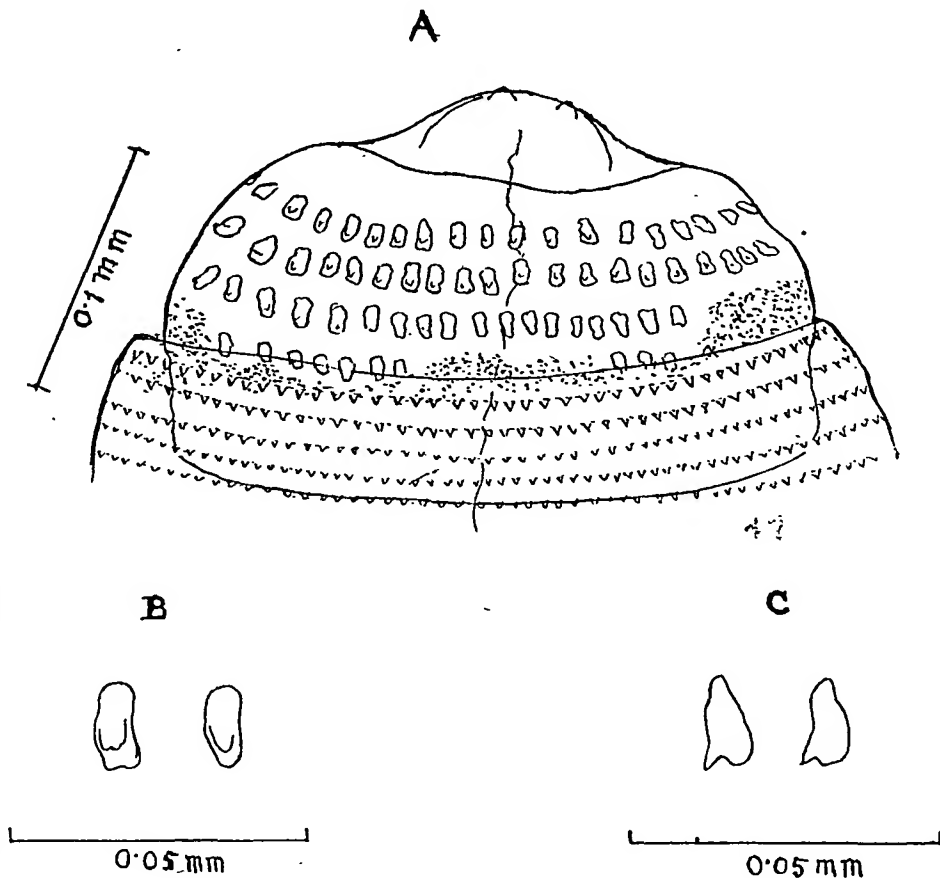


Fig. 2.

- A. Camera lucida drawing of the anterior part of the worm showing the spines.
B. Dorsal view of the spines on the head-bulb.
C. Lateral view of the spines on the head-bulb.

swelling in the throat with dysphagia, and finally, at the point of exit above the right eyebrow, there was considerable swelling of the surrounding tissues causing pressure in the eyeball with lagophthalmos and disturbance of vision.

Gnathostome infection in man may thus produce alarming symptoms, as in this case, and in some of the previous cases, and we draw the attention of medical men to the presence of this infection in Bengal.

Our thanks are due to Captain K. Sen, D.O.M.S., F.R.C.S., for supplying us with the case report and the worm for identification.

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'TROPICAL ULCER' IN EAST KHANDESH

TREATMENT WITH

SULPHATHIAZOLE COD-LIVER OIL PASTE

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It had been brought to the notice of the health authorities in Bombay that cases of chronic ulcer of the skin and underlying tissues, situated mostly on the lower extremities, were occurring in large numbers in East Khandesh district (Bombay Presidency) and that there was a tendency for the ulcers to assume an epidemic form.

East Khandesh district lies in the northerly section of the Deccan tableland, has a population (1941 census) of 1,327,722, an annual rainfall of about 20 inches, the climate being hot in summer and pleasant and bracing in winter.

The investigation, on which the present report is based, was carried out in the K. E. M. Hospital (Civil Hospital), Jalgaon (East Khandesh), in March 1944.

History of the ulcers

Enquiries made at the hospital revealed that cases of chronic ulcer of the skin which were resistant to treatment were seen in different parts of the district, and that they were present mostly in the poorer classes of people. Local medical men were quite definite that numerous cases had been seen by them only during the last 12 months, and that the number of cases was definitely on the increase. The general impression which prevailed was that the incidence of ulcer cases was highest at the end of the last monsoon.

According to the available information during the last six months 6,222 cases of ulcer were treated in the

out-patient department of the several Taluka dispensaries of the district and the Civil Hospital, Jalgaon, and 183 cases as indoor patients. The latter figure includes the cases in the G. I. P. Railway Hospital, Bhhusawal.

The incidence is probably higher than what these figures would indicate. Early cases may not seek hospital treatment. Most cases seek admission into hospitals only when the ulcers are extensive, painful and disabling. The majority of the patients came from the rural areas and, by occupation, they were labourers working in the fields. The railway medical officer informs that ulcer cases were predominantly present in the inferior lower-paid staff (of the railway).

General condition of the patient with ulcer

Most of the patients examined at the hospital, both in the wards and the out-patient department, were poorly nourished, gave a history of repeated attacks of malaria, and were anæmic. Some showed definite clinical evidence of vitamin A deficiency (11 out of 22 cases examined), such as dry papular skin ('phrynoderma'), ichthyotic dry skin, xerosis, pigmentation of the conjunctiva and Bitot's spots. Evidence of 'angular stomatitis' was occasionally seen. The spleen was palpable in some cases. Hæmic murmurs were present at the base of the heart in cases with marked anæmia; œdema of the feet was present in one. The ulcer occurred at all ages and was more common in the males.

Clinical picture of the ulcer

The ulcers were situated on the lower extremities, mostly below the knee. Most patients gave a history of trauma to the legs, particularly from the sharp stumps of 'jowari' plants after harvest. Some noticed a blister before the commencement of the ulcer. The ulcers were generally single, unilateral, and present on the dorsal or lateral aspect of the leg or foot (*vide* fig. 1, plate V). In some cases, both the legs were affected; very rarely, multiple ulcers were present on the same limb. In one instance, an extensive ulcer on the lateral aspect of the leg extending to the thigh was seen.

The ulcers varied in size and shape. The circular ulcers presented a punched-out appearance. Some ulcers were oval or very irregular with crenated edges. Marked variation was seen in the size which varied from 1 to 3 inches in diameter; in one case, the ulcer was 12 inches by 4 inches. While the smaller ulcers involved only the skin and the subcutaneous tissues, the bigger ones were deep, exposing the muscles and tendons. In one case, the upper end of the tibia was visible at the base of the ulcer. The duration of the ulcers varied from 1 month to 6 months.

Cases examined in the out-patient department presented a phagedenic appearance. The

ulcer was covered by a greyish yellow slough and was oozing offensive sero-sanguinous discharge. The edges were undermined and the margins were considerably raised and indurated. The surrounding tissues were oedematous, and the ulcers were extremely painful.

In cases under treatment in the hospital, the base of the ulcer showed unhealthy granulation tissue which bled easily on touch. In some cases, the ulcer showed a tendency to heal on one side and spread on the other. The tissues surrounding the chronic ulcers were indurated and the skin was hyperpigmented. In one case, contracture of the chronic healing ulcer present on the dorsal and lateral aspect of the foot resulted in slight deformity of the foot.

Most cases were afebrile during their stay in hospital. Regional lymph glands were not involved.

Laboratory investigation

(i) *Bacteriology*.—Films of scrapings from the surface of the ulcer and smears from the sloughs and discharge stained by Leishman stain showed in most cases numbers of darkly staining fusiform bacilli and slender spirochaetes (*Treponema vincenti* or *S. schaudinni*) (figs. 2 and 3, plate V). Common pyogenic organisms were rare and, if present, were noticed only in small numbers, compared to the fusiform bacilli. The spirochete was commonly associated with the fusiform bacillus but, in some cases, only the latter was present.

The usual laboratory media were inoculated with the discharge from the ulcers and incubated at 37°C. under aerobic conditions. On culture, the following organisms were isolated: streptococci (*S. viridans*, *S. haemolyticus*, *S. non-haemolyticus*); staphylococci (*S. aureus*, *S. albus*); diphtheroid organisms; an unidentified gram negative short motile bacillus fermenting glucose.

Bacteriological examination of the serous fluid aspirated from the base of the ulcer, by puncturing the healthy skin surrounding the ulcer and pushing the needle beneath the base of the ulcer, was negative for *Leishmania tropica*.

The Wassermann reaction and the Kahn test were negative in all the patients from whom blood samples were collected.

The hæmoglobinized saline medium, described by Row (1912), was inoculated with the blood from the patients. No *Leishmania* was found on culture.

(ii) *Morbid anatomy*.—Pathological examination of sections of an ulcer, obtained by biopsy from the edge, shows vascular granulation tissue at the base of the ulcer covered by necrotic tissue. In between these two layers there is a dense infiltration of leucocytes. The fusiform bacilli are seen in large numbers, sometimes arranged in dense masses, in the superficial parts of the ulcer below the necrotic

tissue. The spirochaetes are seen both at the base and edges of the ulcer.

Treatment

The following treatment was adopted in hospital cases:—

Under general anaesthesia, the ulcer was thoroughly cleaned with weak 'Pemon' solution*, the sloughs were removed; pockets were opened up and the wound mopped dry with gauze. A fairly thick layer of a 'water-in-oil' emulsion containing sulphathiazole and cod-liver oil (prepared by the Department of Pharmacology, Haffkine Institute) was applied, and a pad of cotton wool covered with gauze and impregnated with sulphanilamide was put over the wound and dressed. The paste was prepared according to the formula used by Dikshit and Gardham (1945) (sulphathiazole 12, calcium oleate 2, bees-wax 3, cod-liver oil 60, water 40). The ingredients were separately sterilized and worked into a paste under aseptic conditions. The sulphanilamide impregnated dressings were prepared by soaking cotton wool covered with a single layer of gauze in a hot solution of sulphanilamide and allowing it to dry. In cases showing multiple ulcers or ulcers on both legs, one ulcer was treated as above and the rest were kept as controls and dressed with ordinary saline dressings.

So far, 127 cases of ulcer in different stages of the disease have been treated. One remarkable feature of this dressing was the absence of pain right from the first day of the treatment. Ordinary dressing was so painful that the patients dreaded this procedure. The dressing was renewed once in five days; but subsequent experience has shown that better results were obtained when the dressings were changed once in three days, especially when the discharge was copious. The excessive discharge from the ulcers irritates the surrounding skin and causes an eczematous condition. In less than three weeks, the small ulcers were almost healed and the large ulcers showed considerable improvement (*vide* fig. 4, plate V). In the latter cases, the edges were flattened, the base was covered by healthy pinkish granulation tissue and the surface area of the ulcer was markedly decreased. At this stage, the paste was discontinued, and the clean healing ulcers were dressed with 2 per cent oxalic acid solution. This procedure resulted in a very rapid healing of the ulcers.

In some cases, 10 per cent sulphanilamide paste in vitaminized oil has been used with satisfactory results; but the experience gained by different methods of treatment showed that sulphathiazole paste is by far the best dressing tried for these ulcers.

In addition to the local treatment, the patients were given rest in bed, good food,

* Antiseptic solution containing phenyl mercuric nitrate, prepared at the Haffkine Institute.

shark-liver oil, and fresh lime juice by mouth. Every attention was paid to personal hygiene.

In some cases (8 out of 127 cases), there was a breakdown of the healed scar of the ulcer in about three to four months. In these cases, the original ulcers were large and of long-standing duration and they took a long time to heal. Their general condition was very poor. All of them were poor labourers living on daily wages, and the 'recrudescence' of the ulcer occurred when they reverted to their work and poor diet after hospitalization. In these cases the subsequent healing was very slow.

Discussion

The clinical description of the ulcer given above and the bacteriological and histopathological findings closely resemble 'tropical ulcer' or 'Naga sore' as described in Assam (Roy, 1939) and Coorg (Bopaiya and Rao, 1942). It is a disease of tropical and subtropical regions. Its incidence in India, in places where it was not evident before, has recently been described. Panja and Ghosh (1944) have reported many cases of 'Naga sore' in Calcutta and its suburbs. The high incidence of phagedenic ulcers, particularly 'Naga sore', in starving sick destitutes in Bengal, has been recorded. Evidently the disease appears to be on the increase. It may be mentioned here that the presence of 'tropical ulcer' in East Khandesh has not hitherto been recorded.

A review of the literature on 'tropical ulcer' shows that the causation of the condition is still obscure. There is no direct evidence as yet to suggest that the fusiform bacillus and the Vincent's spirochæte, which are commonly found in 'tropical ulcer', are the causative agent. Most recent workers hold that malnutrition is an important predisposing factor. The occurrence of 'tropical ulcer' has long been noticed among the coolie population employed on tea plantations in Assam and coffee plantations in Coorg. In both areas malaria, hookworm and anæmia are prevalent, and there is much malnutrition. This has been further borne out by the observations of the Calcutta workers. Until July 1943, no cases of 'tropical ulcer' had been noticed at the Calcutta School of Tropical Medicine, but since then a large number of cases have been seen in the starving and sick destitutes in Calcutta and its suburbs. These workers specifically state that cases seen in Calcutta were not imported cases. Our own observations at Jalgaon showed that all cases investigated belonged to the poorer classes who were definitely undernourished.

The greater incidence of the disease in the poorer classes of people, most of whom are ill-nourished and show enlarged spleens and anæmia, suggest that malnutrition, chronic debilitating diseases such as malaria and

ankylostomiasis, and unhygienic conditions play an important part in the rapid spread and delayed healing of the ulcer. It is now well understood that malnutrition delays healing. Therefore, for the proper treatment, it is necessary to improve the general condition of the patient by the administration of good food containing plenty of vitamins A and C, and thus mobilize the defensive forces of the body to promote rapid healing. Shark-liver oil which is rich in vitamin A may be used as supplement to the diet. On account of the painful nature of the disease, it is necessary to admit severe cases in hospitals for treatment. Skin grafting may be necessary in cases where extensive surface is involved. When the underlying tissues are damaged to a great extent, treatment is necessarily prolonged. Hence, people should be advised to seek early treatment.

In all the hospital cases, syphilis was excluded by laboratory tests. Up to the present, the treatment of 'tropical ulcer' has been unsatisfactory. None of the treatments recommended and tried by different workers have borne good results. In our experience, the application of the sulphathiazole paste in water-in-oil emulsion of cod-liver oil has given excellent results. It must be emphasized that the local treatment should be combined with general treatment, especially improvement in the diet.

Summary

(1) The occurrence of 'tropical ulcer' in poor labourers in East Khandesh district of the Bombay Presidency is reported.

(2) Local application of the sulphathiazole paste in water-in-oil emulsion of cod-liver oil in the treatment of the ulcers has yielded encouraging results.

Acknowledgments

Our grateful thanks are due to Lieut.-Colonel S. S. Sokhey for his keen interest and constant help in this investigation, Dr. B. B. Dikshit for placing at our disposal liberal quantity of the sulphathiazole paste for clinical trial, and Dr. V. R. Khanolkar for the photomicrographs.

Addendum: Since writing this report, cases of 'tropical ulcer' have been reported in some of the other districts (Sholapur, Dharwar, Kaira, Karwar, Bijapur) of the Bombay Presidency. Typical cases were also seen by one of us (M. V. R.) in the Bombay suburban district.

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SOLITARY SPLENIC CYST

REPORT OF A CASE

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Our interest in the subject was aroused by the surgical removal by one of us (N. A. A.) of an enormous spleen containing a large unilocular hæmorrhagic cyst. On reviewing the literature we found only two reported cases of splenic cyst in India.

The early literature on the subject is entirely from the Continental journals and the earliest authentic case is in 1829 as mentioned by Andral (Fowler, 1913). Fowler, to whom we owe much of our knowledge on the subject, reviewed the literature in 1913, 1921, 1924 and 1940, bringing the subject up to date. He had collected ninety-eight cases up to 1924 and by the end of 1939 he had reported a total of one hundred and thirty-seven. We have been able to collect twelve more from that date and add one of our own to the list, making a total of one hundred and fifty.

This small number of reported cases substantiates the fact that the cysts of the spleen are rare. Compared with cysts of the ovary, kidney, liver, and other abdominal organs, cysts of the spleen are very uncommon. These cysts are subdivided into three groups: the dermoids, the parasitic and the non-parasitic cysts. The majority are parasitic and are of echinococcal origin. They are most common in Australia, New Zealand and the adjoining islands. Non-parasitic cysts are roughly half as frequent as the parasitic cysts; and they are for purposes of study conveniently divided into true and false cysts.

Pathology.—The splenic cysts have no analogy with the cysts of other abdominal organs, as the spleen, a hæmolymp organ, is structurally different. Retention cysts therefore do not occur. Many valuable articles on the mode of origin and pathology of the splenic cysts have appeared from time to time. Of them the important ones are the views of Aschoff, Beneke and Renggli.

True cysts.—There is however no consensus of opinion on the origin of true cysts. It is generally accepted that they are of congenital origin. For descriptive purposes they have been divided into simple serous cysts, multiple multilocular cysts (or polycystic disease of the spleen) and angiomatous cysts. The simple serous cysts are generally situated on the outer surface of the spleen roughly in the area where the sulci demarcate the primitive lobes. They presumably arise from the cell-nests embedded underneath the splenic capsule during the development of the organ. Pepere suggests that these cysts are developmentally analogous to those in the pelvis of the kidney, ureters and bladder. Beneke, however, contends that these serous cysts are as a result of infoliation of peritoneal endothelium, consequent to the injury to the splenic capsule. Some authors have attempted to differentiate the simple serous cysts of the spleen of peritoneal origin from those of cell-nest inclusions. Little is gained by such differentiation as the histological sections are identical in the two conditions.

The origin of multiple multilocular cysts or the polycystic spleen is likewise hypothetical. Many believe

that they arise from the snared off peritoneal endothelium similar in origin to that of the simple serous cysts, but they possibly arise from ectasia of the lymphatics. These cysts are generally multiple and multilocular and may be either situated on the surface or deeply embedded or both.

The true angiomatous neoplasms are seldom encountered. They are cystic forms of either lymphangioma or hæmangioma. It is said that hæmangioma is not as frequent as lymphangioma. Fink is of opinion that these tumours are dilated cystic spaces arising from lymph channels. The size is generally small and the number scanty.

Dermoids.—The origin of dermoids is no less speculative. There is embryological misplacement of ectoderm within the spleen. The two cases containing both hair and sebaceous material reported by Andral and Kummars are the classical examples. But on reviewing the literature, six more instances (Schneider, 1929; Pohle, 1929; Santy, 1930; Shawan, 1933; Montgomery *et al.* 1938) are found where the tumour is lined by stratified epithelium without other ectodermal structures and are to be included in this group at present.

It is not easy to explain the presence of ectoderm in an organ presumably arising from mesenchyme. Dinand (1930) believes its presence as an autochthonous formation of the mesoderm. Schneider suggests that it may be as a result of inclusion of bits of coelomic cavity capable of forming the epidermis during development.

Pseudocysts of spleen.—These are either hæmorrhagic or serous, and present no lining epithelium. The pseudocysts have been estimated to be four times as common as the true ones. They are most often subcapsular and vary greatly in size. They are generally unilocular and solitary; two-thirds being of hæmorrhagic type and a third of the serous type. The capsular wall consists of thick hyalinized connective tissue with a 'sugar coated' appearance. It is not uncommon to find calcification in the wall. The cysts usually contain blood in various stages of disintegration, the colour varying from reddish brown to slate grey. Cholesterol crystals may be present. Cysts are most often seen in women between the ages twenty and fifty. Trauma seems to be a recognizable factor and in many instances it may be of trifling nature. As large spleens are more apt to be injured, we find malaria and kala-azar as predisposing diseases.

Symptoms.—But for symptoms of pressure, these cysts rarely show anything diagnostic. When they are small there are no symptoms. Intense peritoneal reaction due to trauma may excite acute abdominal symptoms, but generally in almost all the cases reported the patients have consulted the physician for a feeling of heaviness and dragging pain in the left upper abdomen. Digestive disturbances are not uncommon owing to the pressure and encroachment of the spleen. Most of these tumours have been mistaken for a floating kidney.

Treatment.—Cysts of the spleen have been treated by puncture, incision and drainage, or by splenectomy. The last one is the method of choice unless prevented by a mass of adhesions.

Report of a case.—A Hindu female, aged 25 years, was admitted on 9th October, 1943, for pain in the lower abdomen of twelve hours' duration.

The onset of the pain in the lower abdomen was sudden. She had noticed some slight blood-stained discharge per vaginam. There was a history of amenorrhœa for the last three months. On further enquiry subsequent to the operation, it was elicited that about a year ago she had a similar attack. She had had bouts of malaria for some years.

The patient was a fairly well-built woman. No abnormalities were found in other systems.

Local examination.—A tumour was felt extending from the left hypochondrium to the right iliac region. On vaginal examination no discharge was seen. The left fornix was full and tender.

A provisional diagnosis of an ectopic gestation was made, and it was decided to operate upon her immediately.

Operation.—An exploratory laparotomy was done. On opening the abdomen the tumour was found to be cystic swelling merging itself into the spleen. The spleen itself had twisted on its own axis and the splenic notch was facing the left abdominal wall. The tumour with the spleen had a fairly long pedicle. It was ligatured and the spleen with the cyst removed. Since the tumour was not suspected to be a spleen, no pre-operative preparations had been made for collecting the blood and transfusing it. The loss of blood was surprisingly small. It might have been about 50 c.cm. The abdomen was closed as usual and the patient made an uneventful recovery.

During the convalescence it was feared that she might go into stage of extreme anaemia and air hunger, but the recovery was uneventful. It is ten months now since the operation, and we learn that the patient is quite well.

Pathological description.—The specimen consists of a large spleen with the embedded cyst and weighs 2,400 gm. The spleen is greyish in colour and the cyst dull white; the cyst appears as though embedded on the peritoneal surface of the spleen. The spleen proper is more or less oval in shape with shallow indentations. The concavity of the hilum has disappeared and it is recognizable only by a few tags of omentum and blood vessels. The splenic notch is not visible. The spleen proper measures $25 \times 9 \times 9\frac{1}{2}$ cm. The spleen had been removed by ligaturing the splenic artery and the vein at the hilum. There is no evidence of thrombi within these vessels. The capsule of the spleen is thick and is firmly adherent to the underlying parenchyma.

The cyst is globular in appearance and is more than half the size of the spleen; the cyst proper measures $15 \times 10 \times 11\frac{1}{2}$ cm. (see photograph on plate IV). It is uniformly smooth. The capsule of the spleen and that of the cyst appear to be in continuity, except all along the margin of attachment where it is slightly thicker and hyalinized. There are a few tags of mesentery adherent to the inner surface of the cyst.

The cut surface of the spleen is slate grey in colour. The capsule is between 3 and 4 mm. thick. The splenic pulp is firmly adherent to the capsule. The malpighian follicles are indistinct. The trabeculations are increased and the spleen feels fibrous. The cyst is completely walled off from the spleen by its capsule.

The cyst on cutting is found to contain a semi-solid chocolate-coloured substance, which on examination, is found to be blood in various stages of disintegration. There is no splenic tissue.

The microscopic section reveals that the capsule is composed of dense collagen fibres, partly hyalinized, containing a few sinusoids. The sinusoids are filled with red blood cells. Much of the splenic pulp is replaced by fibrous tissue, and the splenic sinuses are mostly obliterated. Malarial pigment is present in large quantity. The malpighian follicles are atrophic and are distantly scattered. The cyst capsule on microscopic examination does not differ by any means from that of the splenic capsule.

Discussion.—Fowler, in his analytical study of solitary hæmorrhagic cysts like the one encountered by us, noticed that seventy per cent of his cases were seen during pregnancy. They were large and solitary. They could be explained as sequelæ to trauma and a subsequent intra-splenic secondary hæmorrhage. He further noticed that in seventy of his collected series, there was a history of antecedent malaria and in twenty-five of his cases there was a history of trauma.

Thus trauma, pregnancy and antecedent disease such as malaria were noticed as predisposing factors in all the cases, either alone

or in various combinations. The case reported was apparently one following malaria, with the possibility of a mild trauma, several months ago.

Conclusion

1. A case report of a splenic cyst removed surgically is presented.
2. About one hundred and fifty instances of splenic cysts have been reported in the medical literature.
3. The histopathology of the cyst is discussed.
4. Enlargement of the spleen on account of malaria with subsequent trauma seems to be the causative factor in the present case.

Acknowledgment

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TYPHUS IN KASHMIR*

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From time to time the existence of typhus has been recorded in Kashmir. In the winter of 1942-43, an epidemic of typhus occurred in Kashmir, and this paper is based on a study of this epidemic.

Kashmir is a large valley at about 5,500 feet surrounded by high mountains 12,000 feet high. In the main valley runs the Jhelum river and the tributaries of this river descend from smaller valleys lying at the foot of the high mountains. These smaller valleys are inhabited largely by people called Gujjars. In the summer they go up the valleys to the mountains for pasturing their cattle and typhus is then little seen. In the winter however when

the mountains and higher valleys become snow-bound, they live in highly congested huts in villages in the small valleys at the foot of the hills. They are all dirty and louse-infested, and in these circumstances typhus occurs and spreads. The Gujjars go to the towns to sell their products and may introduce typhus there; they may also act as a source of infection to other villages in the valleys which are inhabited by other communities.

In Kashmir, the seasonal incidence of typhus, its occurrence mainly in louse-infested people, its epidemiology and mortality, its clinical picture and the results of laboratory tests leave no doubt that the vast majority of cases are of the epidemic louse-borne type. It occurs mainly in the winter. It is confined mainly to the Gujjars and to others who come into contact with them. Whole Gujjar settlements may be affected and whole families in towns or cities. A study of the recent outbreak in Kashmir indicates that the mortality rate varies between 25 and 50 per cent. The clinical picture is that of classical typhus. The typical incubation period, the fever itself, the time of the rash, its distribution, starting on the side of the trunk, spreading and involving the flanks, chest, abdomen and the proximal parts of the extremities, the hands and feet often remaining free, the duration of the fever and its nature, the deaths at the end of the second or beginning of the third week from either pneumonia or peripheral circulatory failure are all seen.

One hundred and forty-six specimens of blood of suspected typhus cases were examined; 67 showed agglutination with OX19 and 6 with OXK and none with OX2. It is frequently found that positives are recorded only at the second or third examination. Savor (Haffkine Institute, Bombay) studied typhus in Kashmir in March 1944 and found agglutination for OX19 only. Guinea-pig inoculations carried out by him showed no Neil-Mooser reaction.

For many years typhus has been considered as occurring in Kashmir but accurate records are very few. A mention is made by Lawrence in his book 'The Valley of Kashmir' published at the end of the last century. Epidemics have apparently occurred from time to time but no accurate records are available. In 1927, an epidemic was reported on either side of Singhpore Pass, and I visited the place and saw numerous cases among the Gujjars. In some fatal cases a suppurative parotitis was seen. Difficulty was then experienced in discerning the characteristic rash partly because of the dark skin of the Gujjars but partly due to lack of careful observation. In the epidemic of 1942-43 and 1943-44, the characteristic rash has been seen by me in many cases. Some cases have occurred among attendants on patients. In one hospital at Baramulla, a lady doctor, a mother superior, and four nurses acquired the infection from patients, and three of them died.

The recent epidemic has occurred in the following areas: Khurhama in Lolab valley, an area notorious for typhus in the past; Kishtwar in Dachhan, Udil in Chenab valley, in Sikh villages in Baramulla and Handwara tahsils, in Uri tahsil adjoining Poonch jagir, in Poonch itself, in the Sindh valley near Ganderbal, in Anantnag tahsil near Kishtwar (Singhpore Pass), at Banihal in Udhampur district. In some places infected blankets were suspected of harbouring the infection. Altogether the number of cases reported to us was 1,526 and 408 deaths occurred, but these figures are probably very incomplete. In the winter of 1943-44, the disease reappeared and this time involved not only the old localities but fresh ones. Badgam tahsil in Baramulla district was the chief focus. Nine hundred and forty-six cases were reported with 320 deaths. During this period immunization against typhus with vaccines was introduced on a limited scale. Among 252 persons inoculated, 16 cases occurred, but in all these cases there was evidence that the infection had been acquired before inoculation; moreover, 9 persons had not received the third injection recommended, 6 having received only one. Two cases occurred in persons fully inoculated but both these attacks were mild with recovery. During the same period, 106 cases and 20 deaths occurred in the uninoculated.

The anti-typhus work consisted mainly of delousing garments by boiling or by heating in a delousing hut where heat was generated between 80 and 100°C.; bathing and delousing of people was also done. Some work was also done with D.D.T. and pyricide 20. Naphthalene was not found of much use in delousing clothes.

TREATMENT OF CHOLERA WITH ATEBRIN

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BRILLIANT and malachite green dyes were found by Panja and Ghosh (1943), bacteriostatic as well as bactericidal to cholera vibrios, but in cholera cases these were not successful, as the dyes were largely discharged by the alkaline contents of the intestine and rendered inactive. Hence a trial was made to find out a dye which would be inimical to the vibrios and at the same time would not be inactivated in the gut.

In a dilution of 1 in 4,000, atebtrin was found bacteriostatic to 10 strains of Inaba sub-type of *V. cholera* and 11 strains of Ogawa sub-type tested; but its effect was nil on 9 strains of para-cholera vibrios and 12 strains of saprophytic vibrios. The dye was also found not bacteriostatic to enteric and dysenteric micro-organisms.

In a dilution of 1 in 4,000, atebirin was found bactericidal in 18 to 20 hours to 21 out of 24 strains of Inaba and 24 out of 24 strains of Ogawa tested. The yellow colour of atebirin was not discharged by the vibrios.

Quinacrine (Sharp and Dohme) in a dilution of 1 in 4,000 was found bactericidal to 15 out of 24 strains of Inaba and Ogawa in 20 hours.

Animal experiments

Guinea-pigs weighing about 350 gm. were starved in the morning, and at about 12 o'clock 5 c.cm. of 5 per cent sodium bicarbonate solution were given intragastrically by our special device to alkalinize the stomach contents. At the same time, 0.25 to 0.5 c.cm. of tincture of opium was injected intraperitoneally and 1/600 grain of atropine subcutaneously so as to paralyse the gut and depress the vagal nerve endings. Then 15 c.cm. of young broth culture of live virulent cholera vibrios were introduced intragastrically and about 2 hours after, 5 c.cm. of filtered atebirin solution 1/100 were similarly given. The control animals were similarly treated but without any atebirin. Preliminary starvation and injection of atropine rendered the intragastric feeding easier, and there was no vomiting or vagus inhibition of the heart during feeding with such an enormous dose of vibrios. Opium was used to allow stay of the vibrios in the gut for a considerable length of time so that the vibrios might exert their pathogenic effect. Blood was taken from the ear vein before atebirin was given to see whether vibrios invaded the blood stream from the gastro-intestinal tract. In some animals, atebirin was given intraperitoneally and in some subcutaneously in small doses.

The control animals died; post mortem—the small intestine was highly congested and found to contain glairy fluid. Vibrios were isolated from heart's blood, gall-bladder, peritoneum and the glairy fluid in the small intestine.

The atebirin-fed animals survived. The atebirin-injected animals died showing an intense hæmorrhagic condition in the lungs. The experiments were repeated by taking 4 animals in each series but as atebirin was found markedly toxic to the animals even by intragastric feeding and as the vibrios were highly invasive in guinea-pigs, further experiments were not uniformly successful.

Human experiments

Twenty cases of bacteriologically proved cholera during an epidemic were given 1 tablet of atebirin every 15 to 30 minutes until 4 or 6 tablets had been given on one day; 2 more tablets were given in a few cases on the next day. As all the cases were admitted late in the collapsed pulseless stage, hypertonic saline had to be given soon after admission into the hospital. An old man, aged 65, passing Ogawa

sub-type of vibrios did not need any saline injection after treatment with atebirin. Nineteen patients survived; one patient died. This patient was a child, one year old and was admitted late in the disease. One child, aged 5, who had passed no urine for 2 days, survived. Six patients were uræmic, and none died. There was no vomiting after atebirin was given except in 2 out of 6 cases with uræmia. All the patients passed urine within 24 hours except 3 with uræmia. The general condition improved within 24 hours in all the patients except in some of those with uræmia. The following statement summarizes the results:—

Five patients—fair (some of them were uræmic); 9 patients—good; 5 patients—very good; 1 patient (child)—died. Improvement in the character of stools was not noticeable in all the patients. In some patients the rice-water character of the stool persisted in spite of improvement in the general condition. In some cases bile reappeared in the stool.

The average amount of saline per patient given was 3.6 pints, but in the cases treated with saline alone, the average was 5.5 pints and death rate was 6.20 per cent.

The number of experimentally treated cases is small.

This report is only a preliminary one, made so that others may try the drug, when available, on early cases. Quinacrine (Sharp and Dohme) was tried on 8 patients only, but the result was not so encouraging as with atebirin.

Summary

1. Atebrin in a high dilution was found bacteriostatic and bactericidal to *V. cholerae in vitro*.

2. The drug was tried in 20 patients of cholera with promising results.

3. Eight patients of cholera were tried with quinacrine, but the results were not so encouraging as with atebirin.

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A NOTE ON TWO CASES OF 'SLIDING' HERNIA

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I HERE report two cases of inguinal hernia in which the anatomical relations were different from usual. 'Sliding' hernia is not very common, but it can occur in the inguinal region on either side. On the right side the cæcum and the appendix may form the posterior wall of the neck and the fundus of the hernial sac,

while on the left side the pelvic or the iliac colon may take up a similar position. Cases are reported where the urinary bladder has also formed the medial relation of the neck of a direct hernia.

The first case was that of a girl, aged 4 years, with an indirect complete reducible left inguinal enterocele. The sac was identified during operation and the round ligament of the uterus was found adherent to the posterior wall of the fundus. In addition, the broad ligament had prolapsed into the inguinal canal and the ovary was the posterior relation of the sac. This caused difficulty in isolating the sac from the ovary and the ovarian ligament. The sac was opened. The contents, small intestine, were reduced into the peritoneal cavity. Instead of transfixion of the neck, the anterior peritoneal wall was sutured to the posterior. The peritoneum was separated from the iliac fossa, and the ovary was pushed back. The further procedure was Bassini's reconstruction of the wall of the inguinal canal.

The second case was in a male, aged 45 years. He had a painful, tense, irreducible swelling in the left inguino-scrotal region with inability to pass flatus and faeces associated with vomiting of six hours' duration. It was a typical strangulated hernia. He was operated on under spinal anaesthesia with stovain. The sac was identified and opened. A large quantity of sero-sanguineous fluid came out. The constriction which was at the site of internal abdominal ring was incised. A long loop of the small intestine was strangulated. As it was viable, it was replaced in the abdomen. Posterior to the neck and the fundus of the sac, a large fibro-fatty mass which contributed to the bulkiness of the swelling did not allow the separation of the peritoneal sac. It was identified as the whole of the pelvic colon with its mesentery in a matted mass firmly adherent to the sac. There was no possibility of returning the pelvic colon to the abdomen. I had to remain satisfied by exteriorizing the colon after the Paul Mickulicz's method. The anterior leaf of the peritoneum was sutured to the upper and lower ends of the colonic loop and the root of its mesentery. The abdominal wall was also similarly sutured. A colostomy rod was passed through the mesentery. The patient had a stormy convalescence due to prolonged hiccup and diarrhoea. On the third post-operative day the whole mass of pelvic colon was excised leaving a colostomy opening in the inguinal region. He will now require anastomosis between the colon above and below to restore his natural passage for faeces. I believe that with a strangulated hernia with a sliding colon it is not possible to reconstruct the inguinal canal adequately.

Conclusion.—Two cases of 'sliding' hernia are reported. In one case the ovary was behind and adherent to the sac. In another the pelvic colon was in this position.

MALARIAL NEPHRITIS

(WITH TWO ILLUSTRATIVE CASE REPORTS)

By P. N. LAHA, M.D. (Pat.)

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Introductory

IN 1891, Marchiafava and Bignami (Editorial, 1942) reported glomerular nephritis in quartan malaria. In 1912, Clark went so far as to say that in the tropics albuminuria was an indication for searching for quartan malarial parasites, or for syphilis! Manson-Bahr and Maybury (1927) and Giglioli (1930) reported nephritis as a complication of malaria caused by *Plasmodium malariae*.

Heilig (1941) and Heilig and Visweswar (1942) have revived fresh interest in this subject. Heilig (1941) reported that in four out of six cases of acute glomerulo-nephritis there was a clear association with malaria, and that all these four cases responded well to treatment with quinine, whereas the other two patients were discharged with evidence of permanently damaged kidneys. Another report of his observations was published in 1942. His main evidence of the malarial origin of the subacute glomerular nephrosis which he described is the response to quinine, and thus he established the excellent diuretic action of quinine in this condition. Heilig is of opinion that his cases were caused by *Plasmodium vivax*.

The patient usually comes with generalized oedema and oliguria. A careful history reveals that he had suffered from malaria before he developed the present complaints. Pallor, slight jaundice, and splenic enlargement are also present. Ascites and pyrexia may or may not be present. The examination of urine shows the presence of albumin, casts, red blood cells and pus cells. The blood shows secondary anaemia, and malarial parasites are usually absent. When parasites are found they are usually *Plasmodium vivax*. Biochemical examination of the blood reveals a rise in urea and cholesterol with a diminished protein content. The oedema does not respond to the usual diuretics, but a dramatic response takes place when quinine is administered.

The absence of any other demonstrable cause for the nephritis coupled with the dramatic response to quinine definitely justifies the diagnosis of malarial nephritis. The areas from where these patients come are free from *Plasmodium malariae*, and moreover cases who have actually shown the presence of parasites in their peripheral blood revealed *Plasmodium vivax* and never *Plasmodium malariae*.

It has been surmised that the nephritis is an allergic phenomenon due to previous sensitization of the kidneys, in susceptible individuals, by foreign protein substances derived from parasite and host tissue destruction resulting from the malarial infection and its cure. This 'kidney-hypersensitivity' is present in only a very small fraction of all malarial infections.

The diagnosis depends on the history of malaria, splenomegaly and the response to quinine in a patient who shows clinical features of subacute nephritis.

The prognosis is usually very good if the treatment is started early. Some patients show a dramatic clinical improvement but the kidneys remain permanently damaged. Some may

die of terminal uræmia in spite of adequate quinine treatment.

Treatment consists of administration of quinine by mouth and if necessary by injection.

Case reports

Case 1.—C., 10 years, Hindu male child, was admitted into the hospital with the complaints of generalized oedema, duration 15 days; occasional attacks of fever, duration 1 month.

On examination.—The patient was pale and weighed just over 6 stones. The temperature was 98.4°F.; pulse and respiration rates of 96 and 24. The blood pressure was 125/105. There was ascites, and the spleen was enlarged 2 inches and was hard. The penis and the scrotum were markedly oedematous. The heart, lungs and nervous system were normal.

Investigations.—Urine: high coloured; specific gravity 1020; alkaline in reaction; albumin present in moderate amount; casts (hyaline and granular), red blood cells and pus cells present. Blood: total red cells 2,180,000; total white cells 4,800; polymorphonuclears 55.0 per cent, lymphocytes 25.0 per cent, large mononuclears 8.0 per cent, eosinophils 2.0 per cent; hæmoglobin 6.9 gm. per 100 c.cm.; no malarial parasites detected. Blood urea 85.6 mg., cholesterol 222.2 mg., and protein 5.5 gm. per 100 c.cm.

Progress and treatment.—He was put on a salt-free diet with restricted intake of fluid. An alkaline diuretic mixture, saline purgative and vapour baths were given for a week, but the patient did not show even the slightest improvement. After a week he was given a mixture containing quinine sulphate 2½ grains per dose, three times a day and all other treatments were completely stopped. About 10 days later his oedema disappeared, there was an increased output of urine, and the size of the spleen diminished. Two weeks afterwards he was investigated again, and the following changes were revealed. Urine: specific gravity 1016; albumin nil; casts, red blood cells and pus cells absent. Blood: total red cells 2,880,000; total white cells 5,800; polymorphonuclears 61.0 per cent, lymphocytes 34.0 per cent, large mononuclears 2.5 per cent, eosinophils 2.5 per cent; hæmoglobin 8.6 gm. per 100 c.cm. Blood urea 55.0 mg., cholesterol 160.0 mg., protein 5.8 gm. per 100 c.cm. Weight 5 stones and blood pressure 105/70.

Case 2.—M., 40 years, Hindu male, cultivator, was admitted into the hospital with the complaints of generalized oedema, duration 1 month; fever with rigor, duration 2 months. The oedema started about 1 month after the onset of the fever.

On examination.—He was afebrile with normal pulse and respiration rates. The weight was 12½ stones, and the blood pressure was 110/70. There was oedema with ascites. The spleen was enlarged 3 inches below the costal margin, and was hard. Other systems revealed no abnormality. There was marked oliguria.

Investigations.—Urine: high coloured; neutral in reaction; specific gravity 1020; albumin present in fair amount; sugar, acetone and bile absent; granular casts, red blood cells and pus cells present. Blood: total red cells 3,230,000; total white cells 8,400; polymorphonuclears 67.0 per cent, lymphocytes 29.0 per cent, large mononuclears 4.0 per cent; hæmoglobin 10.3 gm. per 100 c.cm.; no malarial parasites detected. Blood urea 85.6 mg.; non-protein nitrogen 69.48 mg., cholesterol 400.0 mg., and total protein 6.5 gm. per 100 c.cm. Stool showed a few ova of ankylostoma duodenale. The W.R. was negative. The takata-ara test was strongly positive. Sternum puncture was done but no malarial parasites were found.

Progress and treatment.—He was given a salt-free diet with a restricted fluid intake. The usual routine treatments of nephritis were given to him for a fortnight but there was no trace of improvement. During the next 10 days all these treatments were entirely stopped, and

instead he was given a mixture containing quinine sulphate 5 grains, three doses a day for 10 days. In addition, he was given 3 injections of 5 grains of quinine bihydrochloride by the intravenous route. He showed a fair degree of improvement as evidenced by a reduction of weight to 11 stones and 6 pounds, reduction in the size of the spleen, increase in the quantity of urine, and the disappearance of ascites. Blood: total red cells 3,880,000; total white cells 7,800; polymorphonuclears 61.0 per cent, lymphocytes 30.0 per cent, large mononuclears 9.0 per cent; hæmoglobin 12.1 gm. per 100 c.cm.; no malarial parasites detected. Blood urea 47.0 mg., non-protein nitrogen 43.0 mg., total protein 6.5 gm. per 100 c.cm. These figures indicated a definite improvement. But the urine showed no improvement at all. Urine: high coloured; specific gravity 1020; albumin present in moderate amount; sugar, acetone and bile absent; granular casts, red blood cells and a large number of pus cells present; epithelial cells and uric acid crystals present. This indicated that the damage to the kidneys did not improve much.

After about a month the patient's condition took a downhill course in spite of the above-mentioned improvement. He developed severe diarrhoea which could not be controlled by any treatment. He was again given a trial of quinine by injections but this time it had no effect at all. He developed uræmia (cerebral type) when a lumbar puncture was done and the cerebrospinal fluid showed protein in fine traces, sugar present, chloride 900.0 mg., and urea 285.3 mg. per 100 c.cm. The patient gradually passed into coma and died.

Post-mortem report

Alimentary system normal. Abdominal cavity—2½ ounces of straw-coloured fluid removed. Small intestine—ankylostoma duodenale in the jejunum. Mucosa and wall of bowels normal. Large intestine normal. Liver—48 ounces. Congenital abnormality in the shape of lobulated appearance of left lobe present. Naked-eye appearance was normal. Histology of liver—patches of amyloid degeneration present. Pancreas—normal. Kidneys—capsule could be striped easily, surface was finely granular, cortex-medulla relationship disturbed, at places cortex was very thin, at others it encroached upon medulla. Histology of kidneys—amyloid deposit present in the glomeruli and afferent blood vessels; there was tubular degeneration and casts were present in both the kidneys.

The bladder was full. Generative system normal.

The spleen was enlarged. A patch of perisplenitis present. Histology—marked thickening of the capsule, marked proliferation of trabeculae; lymphoid hyperplasia; amyloid degeneration present.

Lymphatic glands were not enlarged.

Lungs—adhesions present on right and left pleurae. Histology—oedema and emphysema.

Heart well developed, no hypertrophy. Slight fatty infiltration on the right ventricle present. Aorta, coronary vessels and valves normal.

Brain and thymus normal. Bones and joints normal.

Comments

A brief account of malarial nephritis has been given, and two cases are described.

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POST-SULPHAPYRIDINE ANURIA

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CASES of hæmaturia and anuria during the course of therapy with sulphapyridine and sulphathiazole have been reported from time to time. In the General Hospital, Madras, only one case occurred in 1940, and it was reported in the *Indian Medical Gazette* (Sundaram, 1941). A case of post-sulphapyridine anuria with recovery is here reported.

J., an Anglo-Indian, male, aged 62, was admitted on 14th June, 1944, with broncho-pneumonia. He was put on sulphapyridine, 12 tablets on the first day and six daily on the second and third days. He was also given large doses of alkalies and the usual amounts of fluid, as in the routine when the sulpha drugs are prescribed. On the 17th June, after he had had 20 tablets, he developed macroscopic hæmaturia. The tablets were stopped and the quantities of alkalies and fluids were doubled. The urine was clear on the next day. As the patient had been free from fever for the previous three days and as he had to attend his son's wedding, he went home on the 18th evening, against medical advice. He was re-admitted on 19th June, 1944, at 11-30 p.m. not having passed any urine for 28 hours. On catheterization only a few drops of urine were drawn. Although vomiting was prominent, the patient was fully conscious and complained of no pain whatever. He was immediately started on sodium sulphate 4.28 per cent solution intravenously and was given 2 pints of it and 1 pint of 5 per cent glucose saline before 10 a.m. the next day (20th June). As he had not passed urine by then, cystoscopy for ureteral catheterization and lavage was decided upon. Although the procedure and the urgency of carrying it out were fully explained to the patient, he refused to have it done. Alkalies and fluids by mouth and 2 pints each of 5 per cent glucose saline and 4.28 per cent sodium sulphate intravenously were repeated. In addition, atropine 1/100 gr., was given every 8 hours. At 7-30 a.m. on 21st June, 1944, after 60 hours' anuria, the patient passed 6 ounces of urine, and by 10 a.m. the same day he had passed 20 ounces more. He was discharged on 1st July, 1944, having completely recovered.

Results of investigation

Urine : normal when first admitted. The total white cell count was 14,800 on the 15th June and 6,400 on the 20th. The blood urea was 92 mg. per 100 c.cm. on the 20th; 110 mg. on the 21st and 62 mg. on the 24th.

The systolic blood pressure was 136 to 140 mm. and the diastolic 80 to 85 mm. throughout.

A plain x-ray taken on the 20th June showed no stones.

The above case presents certain unusual features which may be further commented upon.

1. Although sufficient fluids were given and retained, hæmaturia set in after only 10 gm. of sulphapyridine. The maximum external temperature of 107° for the summer of 1944 was recorded on 17th June. While no record of the urine output has been maintained, it is difficult to say how much the unduly excessive loss of fluid by way of the skin was contributory to the renal complications.

2. Recovery after 60 hours' anuria has not been reported so far to my knowledge. There are several reports (Benson and Percival, 1942; Kerr, 1943; Thompson, 1943; Laird, 1941) of recovery after ureteral catheterization and Laird (1942) insists that anuria for 12 hours must be regarded as a definite indication for immediate ureteral lavage. A fatal case after 60 hours' anuria has been reported (Carson and Smith, 1942). They had given 5 pints of fluid but make no mention of atropine. In view of Laird's observation that 'the ureteral obstruction may partly depend on reflex spasm of the ureteric wall and that catheterization of one ureter has been successful in re-establishing the secretion of urine from both kidneys' (Laird, 1941), could it be that, in the above case, the repeated injections of atropine counteracted the spasm and made the flow of urine possible?

It may be observed that had the patient not been so obstinate and had he permitted ureteral catheterization, the credit for restarting the flow of urine would naturally have gone to the operation. 'The antispasmodic effect of atropine aids the onward passage of stone—small stones can often be got rid of by giving tincture belladonna' (Price, 1941).

Without presuming to advise the postponement of ureteral lavage beyond 12 hours of the onset of anuria, it is suggested that repeated injections of atropine may be added to the regimen of fluids, alkalies and massage (Flynn, 1943) recommended during the permissible period of 12 hours' waiting. Perhaps, prostigmin (O'Connor, 1940) and trasentin may also be tried.

3. Another remarkable feature was the complete absence of pain or restlessness which had been noted practically in every previous case reported.

4. From the night of 20th June, till the morning of the 22nd, a well-marked third heart sound was heard over the mitral area. His pulse rate never went beyond 80 per minute and his lungs showed no congestion. No overloading of the peripheral circulation was apparent. No prognostic significance could be attached to the proto-diastolic gallop. This observation was considered worth noting here on account of its interest, although no apparent

or imaginable connection exists between this finding and the patient's urinary condition.

I thank Colonel McRobert, Superintendent, General Hospital, for permission to publish the above case report.

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PULMONARY ARTERIOSCLEROSIS PRODUCING UNUSUAL MURMURS AT THE BASE OF THE HEART

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Miraj

PULMONARY arteriosclerosis of Ayerza has received but little attention in recent years in the English medical literature though it still attracts much attention in South America. That it is fairly common in India has long been recognized (Rogers and Megaw, 1939). Our experience bears this out and we have seen three cases proved at autopsy and three other cases diagnosed clinically. Two of these cases showed such unusual murmurs at the base of the heart that they are reported in some detail.

Case 1.—A 30-year-old male Hindu, a railway fitter, was admitted on 26th September, 1942, complaining of swelling of his feet, breathlessness more marked on exertion and cough, all of 5 months' duration. The family history was unimportant. Eight years previously the patient had had pain and swelling of his large joints with fever lasting six months. His recovery was uneventful and complete and he had been able to carry on his work without difficulty until his present illness began. One month ago his complaints had become severe enough to induce him to seek medical aid. He had been admitted to another hospital but, after 20 days of treatment with no improvement, he had taken his discharge and came to Miraj. He had been a moderate alcoholic until eight years ago, and two years ago had had both syphilis and gonorrhœa.

On admission, the physical examination revealed a poorly-nourished patient with orthopnoea, a dusky cyanosis, and anasarca. There was ascites, and œdema of the feet and legs, of the face and all other subcutaneous tissues. The liver was palpable (four fingers) and tender. The lungs were hyper-resonant and there were scattered rhonchi throughout both sides. The cardiac impulse was diffused over the whole precordium. The apex was in the sixth interspace, anterior axillary line. In the second space the left border extended one inch beyond the nipple line, and the right border could be made out 2 inches out in the fourth interspace. The aortic sounds could barely be heard; the pulmonic second sound was accentuated. At the apex there was

a loud systolic murmur accompanied by a thrill. Along the left sternal border, heard well in the second and third interspaces, was a loud, high-pitched systolic murmur, and at the second left interspace near the mid-clavicular line, there was a loud continuous murmur, extending through both diastole and systole but with definite systolic accentuation. In this area, also, there was a well-developed systolic thrill. The fingers were not clubbed. Blood pressure was 100/0 and the pulse was of the collapsing type.

Laboratory findings revealed a moderate degree of secondary anæmia, a negative blood Kahn and a normal erythrocyte sedimentation rate. X-ray taken in the antero-posterior position only showed a very marked enlargement of the heart to the left, with some enlargement to the right also.

The pulse ranged 96-110 during his seven days in hospital and the temperature was normal except just prior to death when it rose to 101.6°F.

Treatment consisted of full doses of digitalin, diuretics and repeated venous section, but the response was nil, and the patient died on 2nd October, 1942.

The autopsy revealed a high degree of atherosclerosis of both pulmonary arteries more marked in the left pulmonary artery, which also showed considerable dilatation. No patent ductus arteriosus was found and the inter-auricular and inter-ventricular septa were intact. There was dilatation of the right auricle and ventricle, and straw-coloured fluid in the pericardium. The valves showed post-mortem change only. The liver showed changes of passive venous congestion, and the spleen was malarial. The lungs showed passive congestion. The kidneys also showed passive congestion and there was some straw-coloured fluid in the abdomen. Microscopic examination confirmed the marked degree of atheroma in the pulmonary arteries, and showed fatty degeneration of the liver.

Case 2.—A 35-year-old Hindu farmer, was admitted on 12th September, 1944, complaining of pain in the epigastrium, occasional bouts of fever and chill, and increasing dyspnoea especially on exertion over the preceding two months. There was no history of venereal disease and the family history revealed nothing of interest. He also denied any other previous illness. Physical examination revealed a cyanosed, well-developed male, lying quietly in bed, but showing signs of dyspnoea on slight exertion. There was slight clubbing of the fingers. The chest wall was somewhat over-distended, there was increased resonance over both lungs, obliteration of the normal areas of dullness, and medium râles at both bases. The area of cardiac dullness was obscured by lung resonance, and the apex was not visible. No thrills could be felt. The aortic and mitral sounds were weak. The pulmonary second sound was exaggerated. Over the base of the heart could be heard a loud double murmur with both systolic and diastolic elements. The murmurs were well heard in the aortic and pulmonic areas but were transmitted upwards and best heard at the right sterno-clavicular joint and below the inner third of the left clavicle, first space. The systolic element was louder than the diastolic on both sides, and on the right side, the diastolic element was louder than on the left. The diastolic murmur was not transmitted down or across the sternum. The pulse was poorly sustained and the blood pressure was 100/55. The liver was slightly enlarged and tender. The Kahn test was 2 plus, and there was a moderate degree of secondary anæmia. The venous pressure (direct method) was 7.5 c.cm. and the arm to lung (ether) circulation time was 8 seconds. X-ray showed slight enlargement of the heart both to the right and to the left with diffuse dilatation of the aortic arch. The right pulmonary artery was definitely dilated and all peribronchial shadows were increased. Fluoroscopy confirmed these findings and revealed considerable pulsation of the pulmonary arteries. The electro-cardiograph showed slight right axis deviation only.

Therapy was purely palliative and, after three weeks, he felt sufficiently improved to ask for and obtain discharge.

Comment

That systolic murmurs at the base of the heart can be produced by dilatation of the pulmonary arteries has long been recognized (White, 1937; Sodeman, 1944). That this dilatation and murmur may be due to pulmonary atherosclerosis has also been commented upon. However, it has not been possible to find any reference to this condition producing a double murmur at the base as was the case in our first patient, and as was suspected in our second patient. White (1937) mentions three causes of continuous murmurs at the heart base, (a) physiological venous hum, (b) patency of the ductus arteriosus and (c) arterio-venous aneurysm—as a rupture of an aortic aneurysm into the pulmonary artery or vein or into the superior vena cava. In our first case, the clinical diagnosis had been that of ductus arteriosus patency probably associated with an inter-auricular or inter-ventricular septal defect but a very careful search at autopsy failed to reveal either; only the pulmonary atherosclerosis with marked dilatation of the left pulmonary artery was found. It was on the basis of our experience in this case that signs of pulmonary atherosclerosis were carefully searched for in the second case. Still to be explained, however, is the poorly sustained pulse found in both these cases. In our case 1, the aortic valve was quite normal at the autopsy.

Summary and conclusions

1. Pulmonary atherosclerosis is fairly common in India.
2. Two cases of pulmonary atherosclerosis, one proved at autopsy, causing double murmurs at the base of the heart, are reported.
3. Unusual systolic, double or continuous murmurs of gradual onset at the base of the heart in adults should arouse the suspicion that pulmonary atherosclerosis may be present and lead to a careful search for the same.

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TROPICAL PYOMYOSITIS (BUNG-PAGGA'S DISEASE)*

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THREE cases of tropical pyomyositis were recently admitted to this hospital. All were soldiers, and their ages were 20, 21 and 26 years. One was perfectly healthy prior to the onset of

the disease; one had concurrent B.T. malaria infection, and the third had concurrent bacillary dysentery exudate. There was no history of trauma in any of the cases.

The clinical picture in these cases was fairly typical of the disease—irregular pyrexia, 100 to 104°F. of a remittent type, with profuse sweating, deep-seated intramuscular multiple abscesses at different sites and a moderate leucocytosis were the main features. There was moderate generalized enlargement of the lymphatic glands; spleen and liver were not enlarged. There was progressive loss of weight. No septic foci were detected on clinical examination. The abscesses were distributed as follows in the three cases—

Adductor of the thigh	3
Posterior axillary fold	2
Serratus magnus	2
Rectus abdominis	1
Oblique muscle of the abdominal wall	1
Gluteii	1
Biceps	1

Textbook description of the disease.—Tropical pyomyositis is a disease of controversial aetiology. It was first recognized by Scott in Jamaica in 1912 and in the same year by Kulz in Cameroons.

It is characterized by deep-seated intramuscular abscesses, often leading to metastatic pyæmic manifestations. Formerly it was thought to have some relationship with filariasis. The view now held is that it is an independent condition.

Two forms usually occur: (1) hard indurated painful inflammatory swellings, situated deep in the muscular tissue, which are caused by a collection of serous fluid, (2) wide and extensive suppuration.

The gastrocnemii, adductors of the thigh, serratus magnus and latissimus dorsi are the favourite muscles affected. Recurrence is a feature.

Investigations.—The total w.b.c. count was moderately raised. It varied in different cases and at different phases of the disease between 8,000 and 17,500 per c.mm. The differential count showed a preponderance of polymorphs in all cases and a gradually rising monocytosis in the third case (without malaria or dysentery).

Pus was thick and the colour varied from yellow to chocolate brown in different abscesses; the organisms found were *Staphylococcus aureus* and *Streptococcus pyogenes*.

The blood films were negative for filaria.

The Wassermann reaction was negative.

Treatment.—No therapeutic measures appeared to have any effect on this self-limited disease. Sulphathiazole was the routine drug used; it did not help much. Some of the abscesses were opened and drained; others subsided spontaneously. The time of complete subsidence was 1, 1½ and 3½ months in the three cases.

The special points that emerge from observation of these three cases are:—

(1) The condition does not seem to be caused by pyæmia. Signs of marked toxæmia were absent and blood cultures were sterile; all the cases recovered; the abscesses were all localized in the muscles; there were no signs of abscess formation in the lungs, spleen, liver, joints, etc.

(2) The muscles affected were not those which are usually most used.

*Paper has been rearranged by the editorial office.

(3) Monocytosis and mild generalized glandular enlargement may be a feature of this condition.

I am thankful to my O.C. Colonel A. Rosenbloom for allowing me to publish the résumé of the clinical notes.

A SIMPLIFIED LEUCOTOME

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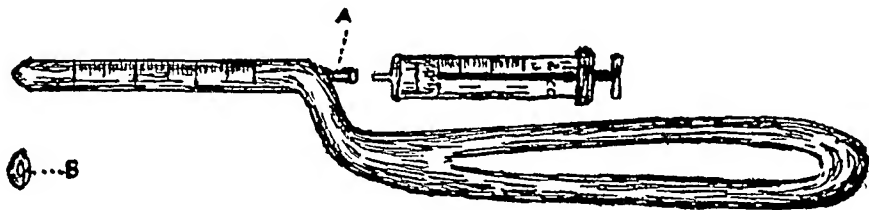
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FREEMAN and Watts recommended the use of a Killian's nasal elevator in the performance of pre-frontal leucotomy in mental disorders. A combined suction and cutting instrument was first described by McGregor and Crumbie (1942). This instrument was used by Rao and Govindaswamy (1944) in a series of cases, and during operation in one case, the rotating blade slipped inside the brain from its mounting, and the instrument had to be withdrawn from the substance of the brain with the blade open, after an extensive resection of the skull; the laceration to the brain and dura mater was considerable, and there was a great deal of hæmorrhage. To obviate accidents from such a complicated leucotome, a simplified instrument has been devised.

This is essentially a Killian's nasal elevator as recommended by Freeman and Watts, but the blade is hollow, with an attachment at its proximal end to fit a record syringe. The outside of the blade is graduated in centimetres to indicate the depth to which the instrument has been introduced. The instrument was made for us by a local silversmith (see figure).



Simplified leucotome (diagrammatic).

A. Attachment for syringe.
B. Cross-section of blade.

The advantages of this leucotome are:—

(1) It is simple in design and has no complicated mechanism to get out of order.

(2) It has all the advantages of the complicated McGregor and Crumbie leucotome. It can be ascertained whether the instrument has entered the ventricle of the brain or not, and the sectioning of the white matter can be done

in one manœuvre. This eliminates the use of a separate needle.

(3) The instrument can be made by any silversmith.

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CEREBRAL EMBOLISM FOLLOWING ANTRUM PUNCTURE

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Introduction

A WORKER in the nose department of a largely attended general hospital has not to wait long before he comes up against some unpleasant accident following such a simple procedure as antrum puncture, or an attempted puncture. Fortunately most of these accidents are trivial. Mishaps like the entry of the trocar into the opposite wall resulting in infiltration and emphysema of soft parts of the cheek and orbit are such as can usually be avoided through judicious care, and tend to decrease as the experience of the operator increases. There are other accidents, however, that are beyond the operator's control; examples are cocaine poisoning, or the reflex irritation of vagus through the maxillary division of the fifth cranial nerve. Under the same heading, but in a more serious category, are grouped cases due to vagal shock or apoplexy resulting in death, and cases of air embolism which may or may not be fatal.

Air embolism, first reported by Hajek (1926) in 1907, is one of the rare complications following

antrum puncture. The following case of cerebral air embolism is illustrative:—

Case report

Mrs. K. D., 22, Hindu female, married (one child), attended the Ear, Nose and Throat Out-patients Department of the Mayo Hospital, Lahore, on 28th October, 1944, complaining of cough, worse at night, following

an attack of cold in the head a fortnight before. As nasal examination warranted, a proof puncture was done on the right side under local anaesthesia (10 per cent cocaine plug for 15 minutes). The introduction of the trocar and canula through the inferior meatus was accomplished without much resistance. There was no bleeding. With the compression of the air bulb of the Higginson's syringe, which was done without undue pressure, the patient complained that she was feeling very ill. The syringe was immediately disconnected, the canula removed, and the head of the patient lowered. As the head was lowered she had a generalized clonic convulsion starting from the left hand and spreading to the entire body, the legs being involved last. During the convulsions she became unconscious; the facies were ghastly pale. The head deviated to the right, the pupils were dilated but reacting to light, the pulse was feeble. After about two or three minutes, the convulsion disappeared but all the four limbs remained rigid for about 35 minutes, after which the corneal reflex reappeared, the pupils tended to assume their normal size, and the patient recovered consciousness. Examination of the nervous system at this stage revealed nothing except but the paralysis of the left arm. She was admitted into the hospital for observation. The paralysis lessened considerably after 3 hours but disappeared completely only after 17 hours. During recovery there was a slight rise of temperature (99°F.); she complained of headache and vomited several times.

At the onset of symptoms, the patient was kept warm, smelling salts were presented, injections of $\frac{1}{4}$ c.cm. of 1 in 1,000 adrenalin hydrochloride were given hypodermically, and 1.7 c.cm. of coramine was given intramuscularly.

Discussion.—In the differential diagnosis, hystero-epileptiform convulsions could be ruled out at the outset. Similarly a spasm of one of the cerebral arteries need not be considered in view of the absence of evidence of cardio-vascular degeneration. A septic embolus from the antrum would have been arrested in the lungs, and in any case would not have resolved so quickly and so completely within seventeen hours. A careful examination of the heart did not reveal any disease, and hence cardiac vegetations could not be a possible source of the embolus. The mode of onset of the symptoms and the speedy and complete resolution of the lesion in the brain point to an air embolus as the cause.

Source of the embolus.—The air embolus enters the general circulation through a puncture in one or more of the veins draining the maxillary sinus. It may produce cardiac and respiratory symptoms, or, as in this case, nervous symptoms, according to the principal or accidental paths followed by the embolus. The course of the embolus causing respiratory and cardiac symptoms is easily explained; but more difficult to understand is the transfer of the embolus from the venous into the arterial system, in the absence of a patent foramen ovale, thereby causing lesions in the central nervous system, such as occlusion of the central artery of the retina (Hajek, 1926) or one of the branches of the cerebral arteries as in the present case. It is believed that an air embolus can pass through the lung without producing corresponding symptoms and lodge in the cerebral circulation (Lewison, 1925).

Acknowledgments

We thank Dr. K. L. Wig, M.R.C.P., for kindly examining the case and establishing the diagnosis, and Dr. A. Rashid, D.L.O., for help during management of the case.

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INVESTIGATION INTO THE TOXICITY OF LARGE VOLUME SERUM TRANSFUSIONS

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THE investigation was undertaken with the object of determining the toxicity or otherwise of liquid serum. We had been using liquid serum with satisfactory results for the past two years in quantities up to 1,000 c.cm. Brigadier H. L. Marriott, R.A.M.C., consulting physician to the Medical Directorate, G.H.Q., however pointed out that, in order to determine toxicity, larger volume transfusions were required and that the rate of transfusion must be rapid.

It was consequently decided to transfuse a series of cases with serum under agreed standard conditions. It should be noted that the investigation was undertaken for this purpose alone, and that in certain cases the technique used could not be described as logical—the use of other fluids being indicated. For example—case 19 obviously required blood, and some of the cases would have benefited by the more active treatment of dehydration.

Under these conditions it could reasonably be expected that, if serum was toxic, its effects would be enhanced, and manifestations of toxicity would be increased.

It is generally accepted that plasma is innocuous when given in large quantities, and the majority of British workers favour this substance. The majority of American and Canadian workers, however, favour serum. Plasma is more difficult to prepare and, as it is diluted with sodium citrate solution, it contains less protein (approximately 30 per cent) than serum. Serum on the other hand is easy to prepare and maintain, and is concentrated, but it is said to contain toxic bodies, produced at the time of clotting, which cause reactions, many of which are severe and may be fatal.

From the clinical point of view we have no particular bias towards either substance, but, having to process the substance ourselves, we naturally prefer the one easier to prepare and maintain, and for that reason, and as the clinical results have been satisfactory, have used more serum than plasma. The views of current workers on plasma and serum are set out in 'the report of the Blood Transfusion Association connecting the project for supplying blood plasma to England—January 31st, 1941'. They indicate that the trend of current opinion is to consider serum as innocuous.

The standard adopted for experimental investigation

- (1) The transfusion volume to be not less than 1,000 c.cm. of undiluted liquid serum.
- (2) The rate of transfusion for the first 500 c.cm. to be 10 minutes, second 500 c.cm. 20 minutes and third 500 c.cm. 30 minutes. This has been adhered to so far as circumstances would permit.
- (3) The patient must have lost blood and be in the clinical state of shock.
- (4) The systolic blood pressure to be 90 mm. Hg. or below and/or falling.

Symptoms and signs of toxicity

- (1) A fall in blood pressure following transfusion and/or failure to raise the lowered blood pressure with further transfusion of serum.
- (2) Reactions.
- (3) Increase in pulse and respiration rate.
- (4) Death.

Difficulties immediately arose in assessing toxicity. The type of cases treated was of the poor class, ignorant and alarmed at having to enter hospital. In this class we know from experience that any unusual manipulation causes considerable mental stress and raises the respiratory and pulse rates. Rigors due to non-pyrogen-free water and imperfectly cleaned apparatus may occur with ordinary saline transfusions, and it is difficult to estimate whether they are due to these causes, or to serum. We considered the most reliable signs of toxicity to be a fall in blood pressure, and doubted the evidence of the mild reactions as being an indication of serum toxicity. All the cases transfused were 'emergencies' and fall within a class of case described in the annual report of this hospital for 1937, i.e. cases examined vaginally outside the hospital and admitted with membranes ruptured or unruptured and not attended to antenatally.

This class formerly filled us with pessimism at the inadequacy of our treatment and the lamentable results. The situation has however changed, and we considered this to have been brought about by early transfusion with serum. If serum were toxic, we would reasonably expect our mortality rate to rise as a result of treatment. In treating a series of cases in which formerly we would have considered a

30 per cent recovery rate as very satisfactory, we have a recovery rate of 91.6 per cent, and after three years' experience we still remain optimistic.

Discussion on 24 cases transfused

The smallest quantity transfused was 1,000 c.cm. and the largest 2,600 c.cm. It must be pointed out that, due to the desire to obtain definite information regarding the toxicity of serum, some cases were transfused in a manner that could not be described as orthodox—in that we deliberately withheld whole blood or glucose saline when they were, in our opinion, indicated. In most of the cases transfused, we would have ordinarily at first given blood and then followed up with serum. In spite of this omission, the results have been surprisingly good, and convinced us that even in cases that had lost a considerable amount of blood, it was possible to resuscitate the patient and save life. If this observation is correct and confirmed by other workers, its practical application is of considerable importance in this country for the following reasons. In transfusion work with any substance, speed is essential. After it has been decided that a patient's condition is such that transfusion is the method of treatment, the longer the delay, the higher the mortality. We consider that 15 minutes after the decision has been made to transfuse, the canula should be in the vein and the fluid entering. Even with a well-organized blood bank, some delay is inevitable, and where no blood bank is available, the obtaining of a suitable whole blood may result in delay of up to 24 hours, and the transfusion in most cases will be too late.

It is comparatively easy to make the necessary arrangements for serum to be instantly available, and, if it can resuscitate cases of severe hæmorrhage and keep them going until suitable whole blood is available, it is of the greatest practical value. We were aware that serum was valuable in cases of moderate hæmorrhage but its action in cases of severe hæmorrhage has greatly impressed us.

Clinical results of transfusion

As the transfusion proceeded and blood pressure rose, patients became quieter and in some cases fell asleep. Vomiting ceased and fluids were retained orally. The blanched appearance of the face disappeared and the general condition markedly improved.

Toxic symptoms

Blood pressure.—In no case was there a fall of blood pressure during or immediately following transfusion. Any subsequent fall responded to further transfusion with serum. Cases 10 and 19, both of whom died, indicate the effect of serum on the blood pressure. Both cases were unfortunately over-transfused.

TABLE
Summary of 24 cases

Num- ber	History and condition on admission	Treatment and effects							
		G.S. 500 c.cm.	S. 500 c.cm.	S. 500 c.cm.	1½ hrs.	G.S. 250 c.cm.	G.S. 500 c.cm.	3 hrs.	
1	Premature labour. P.P.H. Pt. 2. Manual removal of placenta. B.P. 60/50. P.=152. R.=38.	B.P. 68/40 Pulse 142 Resp. 34	80/48 144 34	90/54 144 34	80/50 128 34	80/50 120 32	1 hr. 88/50 122 32	88/48 128 30	
2	Retained placenta. P.P.H. Pt. 2. Manual removal. Rapid fall of B.P. 48/38. R.=32. P.=100.	B.P. 55/35 Pulse 120 Resp. 32	B. 300 50/30 120 34	S. 500 50/38 116 40	50/35 122 38 Manual removal, hæmor- rhage Pt. 1.	S. 500 ? ? Hæmor- rhage 12 oz.	S. 500 ? ? Hæmor- rhage 8 oz. Rigor.	90/55 164 40 32 S. 600 ½ hr. 62/38 140 30	1½ hrs. ½ hr. 72/43 80/45 148 142 48 3 hrs. 90/50 108 26
3	Abortion. Severe hæmorrhage. Fall in B.P. from 92/68 to 70/50.	B.P. 70/50 Pulse .. Resp. ..	G.S. 300 70/50	S. 500 70/50 82/50 82	½ hr. 1 hr. 96/60 86 28	S. 500 102/62 100 26	1½ hrs. 114/68 106 21	4 hrs. 98/60 84 26	
4	P.P.H. 16 oz. B.P. 64/40.	B.P. 72/50 Pulse 126 Resp. 28	S. 500 86/42 120 40 Urti- caria legs.	S. 250 100/58 110 54 Rigor.	½ hr. 118/60 118 46	6½ hrs. 108/50 116 28			
5	Hæmorrhage + + +. B.P. 60/40. P.=130. R.=36.	B.P. 60/40 Pulse 140 Resp. 42	S. 500 70/40 142 42	80/50 136 38	S. 600 85/50 128 32	90/50 110 30	S. 500 90/50 110 30	95/50 110 30	
6	P.P.H. 20 oz. Fall in B.P. from 118/68 to 56/40. P.=130. R.=31.	B.P. 58/32 Pulse 136 Resp. 42	S. 500 92/50 116 30	108/54 124 37 Urti- caria	½ hr. 112/65 124 32				
7	Placenta previa. Hæmorrhage + + +. Fall in B.P. from 90/58 to 78/52.	B.P. 100/50 Pulse 108 Resp. 25	S. 500 110/60 106 34	S. 300 110/60 108 32	2½ hrs. 118/70	1½ hrs. 110/80 104 ..			
8	B.P. fell from 102/82 to 76/44. P.=164.	B.P. 76/44 Pulse 164	S. 500 106/64 ..	S. 500 104/68 132	1 hr. 100/70 120	8 hrs. 92/70 112			
9	Hæmorrhage + + +. Fall in B.P. from 94/64 to 78/58.	B.P. 78/58 Pulse 126	G.S. 500 100/64 130	S. 500 94/68 136	G.S. 500 78/50 124	S. 500 78/50 124 Rigor	2½ hrs. 100/60 140	6½ hrs. 106/68 120	

Blood = B.

Serum = S.

Glucose saline = G.S.

TABLE—contd.

Num- ber	History and condition on admission	Treatment and effects									
10	Ruptured uterus—2 days in labour. Fall in from 120/76 to 94/64.	B.P. 96/64 Pulse 148 Resp. 38 Operation.	S.1500 132/60 168 50	3½ hrs. 138/54 140 42	1½ hrs. 136/52 140 38	4½ hrs. 115/54 144 40	} Died.				
11	P.P.H. 32 oz. from 124/94 to 40/20. P.=128. R.=30.	B.P. fell Pulse .. Resp. ..	S.500 92/54 104 24	S.500 118/54 130 22	1 hr. 120/55 136 28 Urticaria	1½ hrs. 100/56 136 30					
12	P.P.H. 25 oz. P.=130. R.=38.	B.P. 60/40 Pulse 130 Resp. 38	S.500 90/46 140 46 Urticaria	1½ hrs. 80/35 160 48 Rigor	5 hrs. 92/65 130 38	5 hrs. 116/64 110 ..					
13	Ectopic pregnancy. B.P. 76/58. P.=140. R.=28.	B.P. 76/58 Pulse 140 Resp. 28 Operation.	S.500	S.500 104/64 120 26	S.500 85/40 124 24	¾ hr. 78/35 110 30	1 hr. 95/50 122 24	1 hr. 100/50 110 24			
14	Obstructed labour. and pulse not recordable.	B.P. Nil Pulse Nil Resp. 38	S.500 80/? Nil 42	S.500 138/106 124 44	S.300 150/108 120 44 Cranio- tomy.	130/92 130 42	1 hr. 140/92 116 40 Urticaria	1 hr. 120/90 122 42	3½ hrs. 90/60 100 45		
15	P.P.H. Pulseless. B.P. 50/40.	B.P. 65/45 Pulse 120 Resp. ..	S.500 100/60 120 30	S.500 100/60 120 30 Urticaria Rigor	90/45 126 ..	1 hr. 102/64 136 28	2 hrs. 104/68 120 22				
16	Subtotal hysterectomy right and left. Salpingo-oophorectomy. Three hours after operation, pulse imperceptible. B.P. 56/30.	B.P. 56/50 Pulse Nil Resp. 22	S.500 96/60 96 24	½ hr. 96/70 96 23	S.300 ½ hr. 100/70 114 24	2 hrs. 104/64 110 24					
17	Central placenta previa. Hæmorrhage +++ before admission. Cæsarean section. B.P. 90/70 falling to 70/50 after operation.	B.P. 70/50 Pulse 140 Resp. 24	S.500 80/55 132 26	S.500 98/62 128 26	3½ hrs. 94/60 124 24	2 hrs. 102/62 120 22					
18	Central placenta previa. Fall in B.P. from 106/68 to 70/50. Pulse uncountable.	B.P. 90/50 Pulse Nil Resp. ..	S.500 90/70 Nil ..	S.500 104/85 Nil ..	124/80 Nil Slight rigor.	¾ hr. 106/56 184 30	B.500 112/70 Cæsarean section.	¾ hr. 72/38 160 42	B.400 80/50 156 36	1½ hrs. 114/88 130 30	
19	P.P.H. 56 oz. Manual removal, placenta very adherent. B.P. 86/42. P.=140. R.=36.	B.P. 86/68 Pulse 144 Resp. 40	S.500 Slight rigor.	S.500	S.200 125/75 Pulse uncountable	1 hr. 86/50 55	1½ hrs. 50/35 60	S.500	B.450 98/55 138 36	Gasping. Cyanosis. Died.	

Blood = B.

Serum = S.

Glucose saline = G.S.

TABLE—concl'd.

Num- ber	History and condition on admission	Treatment and effects								
		G.S. 250	S. 500	S. 500	G. 500 25 min.	G. 500	1½ hrs.	S. 200	40 min.	6½ hrs.
20	P.P.H. B.P. not recordable.	B.P. ..	60/38	70/45	82/52	88/50	70/35	..	80/48	102/53
		Pulse	100	128	120	148	..	140	120
		Resp.	25	40	40	36	..	34	30
21	P.P.H. B.P. 70/46. Pulse irregular. R. = 26.	S. 500 B.P. 105/75	S. 500 104/72	25 min. 1 hr. 106/70	4½ hrs. 86/52					
		Pulse 80	..	96	116	98				
		Resp. 26	36	34	34	26				
				Rigor						
				Temp- erature 100.8°F.						
22	P.P.H. 25 oz. Pulse barely perceptible. B.P. 58/?. Respiration rapid and not countable.	S. 500 B.P. 58/?	S. 500 105/70	120/60						
				Rigor						
					District case. Conditions made detailed recording impossible.					
23	Hæmorrhage +++. B.P. 76/50. Pulse = nil.	G. 375 B.P. ..	S. 500 80/62	S. 500 92/72	1 hr. 100/65	3 hrs. 78/50	G. 500 1½ hrs. 80/50	6 hrs. 80/40		
		Pulse ..	90	96	144	140	144	132		
		Resp. ..	20	20	38	36	30	32		
					Rigor					
24	Hæmorrhage 30 oz.	S. 500 B.P. 58/30	S. 500 78/38	S. 500 80/48	G. 500 92/48	2½ hrs. 110/55	2 hrs. 114/72			
		Pulse 104	100	120	..	106	104			
		Resp. 22	22	26	26			
			Manual removal of pla- centa.							

Blood = B.

Serum = S.

Glucose saline = G.S.

Note.—Unless otherwise mentioned the blood pressure, pulse and respiration were recorded every 15 minutes. To economize in space all readings are not recorded.

Reactions.—I. Urticaria occurred in 6 cases (25 per cent) and readily responded to adrenalin.

II. Rigors: 10 cases:—

(a) 8 mild—slight shivering, and temperature up to 100°F., duration of rigor up to 30 minutes.

(b) 2 severe—marked shivering, temperature over 100°F., rigor lasting for more than 30 minutes.

III. Respiration.—Three patients (8, 9 and 12) experienced respiratory distress, i.e. difficulty in breathing, tightness of chest, coughing and sneezing; all readily responded to adrenalin. All three cases were given serum which was hæmolyzed and which was diluted with one-third non-hæmolyzed serum. The degree of hæmolysis was not ascertained, but the colour was dark red. Whether the above symptoms—which were considered to be allergic and responded immediately to adrenalin—were influenced by the hæmolyzed serum we are not able to say.

Mortality

Two patients died.

Case 10.—Admitted in a dying condition. 4th para; previous 3 labours normal; had been in labour 49 hours. Uterus was ruptured—cause of obstruction, hydrocephalic foetus. Serum transfusion improved the general condition. Total hysterectomy then performed. Two prominent features were present in this case: (1) our operative mortality in this class of case is high (50 per cent); (2) the blood pressure was high throughout and protein transfusion was contra-indicated on the blood pressure evidence.

Case 19.—Had lost 56 ounces of blood during the 3rd stage. Manual removal of the placenta. This case should have been transfused with whole blood. The serum however raised her blood pressure.

In the above two cases we were unable to conclude that serum had any toxic effects.

Conclusion as to toxicity

Excluding cases 8, 9 and 12, no symptoms or signs were recorded that could be regarded as of toxic origin, and in our opinion the above three cases presented an allergic syndrome that readily responded to adrenalin.

The outstanding and impressive feature in this series of cases is not the occurrence of reactions or anything that indicated ill effects as a result of transfusion, but the remarkable way in which the patients, whose conditions appeared hopeless, recovered.

The series of cases is admittedly small, but the conditions were such that if serum were toxic, one would have expected marked manifestations of toxicity.

An analysis of the results leads us to the conclusion that, so far as this series of cases is concerned, serum was non-toxic. This coincides with our previous clinical experiences of the previous two years when using serum in up to 1,000 c.cm. quantities.

SULPHONAMIDE AMBLYOPIA AND ITS TREATMENT WITH NICOTINIC ACID

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Divisional Medical Officer, East Indian Railway

In November 1943 an ophthalmologist was confronted with a case of total blindness in a girl following prolonged use of M&B 693. On my suggestion she was treated with nicotinic acid, which resulted in complete restoration of her sight. In March 1944 Hollis and Baty (New England) reported a case of a 6 weeks' old child treated with sulphathiazole for meningitis due to the colon bacillus. The drug sterilized the cerebro-spinal fluid in a week but left the child totally blind. The report of Hollis and Baty's case reached me by August 1944. In the same month another case of complete blindness of about four months' standing following the use of a sulphonamide given for puerperal sepsis was brought to my notice. This case is still under treatment with not much hope of success. In all the three cases the cause of amaurosis is optic atrophy of the toxic type. There is practically no mention of this manifestation of sulpha drug poisoning in the literature, though visual disturbances with optic neuritis due to sulphonamides have been recorded as early as 1937 (Bucy). This crippling toxic effect of so widely used drugs does not appear to be very uncommon. It fortunately appears to be amenable to nicotinic acid therapy if given in very early stages but is generally resistant to ordinary routine treatment in all stages and does not appear to yield even to nicotinic acid if its exhibition is delayed for a few months.

The data of the two cases that have come to my notice are given here:—

Case 1.—Muslim girl, aged 8 years, was operated on for mastoiditis; a sinus persisted. M&B 693, three tablets and sulphanilamide dressing locally, were given daily for about a month. The sinus did not heal but the girl developed a sudden loss of vision on 6th November, 1943. She was examined at the M. D. Eye Hospital, Allahabad.

11th November, 1943. 'Eyes: (1) no paralysis of any ocular muscle detectable; (2) pupil—somewhat dilated and inactive; (3) media—clear; (4) tension—18 mm.; (5) vision—R/E—no PL (perception of light); L/E—PL? No PR; (6) fundus—(a) optic disc—white; margins somewhat blurred; blood vessels near the disc narrow in calibre, otherwise normal. Lamina cribrosa—not obliterated; (b) general look of fundus—not much change; Kahn test—negative.'

Acetylcholine $\frac{1}{2}$ c.cm., potassium iodide and sodium salicylate given internally, and oleate of mercury to temples. There was no improvement. I then advised nicotinic acid. The girl was given 50 mg. intramuscularly and 100 mg. twice a day orally. In eight days, PL and PR restored in both eyes. On the tenth day, vision—hand movements at 6 inches to 9 inches. On 1st December, 1943, finger counting at 6 inches. In twenty-five days, she could walk about easily and her disc assumed a very light pink colour. Injections of nicotinic acid were stopped but 100 mg. was given orally twice daily. In five weeks her optic disc became absolutely normal and her vision in both eyes was 6/12.

Case 2.—Muslim female, aged 28 years, had puerperal sepsis and was given a sulphonamide, 4 tablets a day for four days. On the fourth day she felt haziness of vision and in about ten days lost her sight completely. She tried various treatments and appeared at M. D. Eye Hospital, Allahabad, after 4½ months.

Examinations.—Eye: (1) tension—normal; (2) media—clear; (3) fundus—(a) optic atrophy (white disc with thin vessels, (b) lamina cribrosa—quite clear. No PL.

Treatment.—50 mg. intramuscularly (3 injections) and 300 mg. of nicotinic acid orally a day for one week. No improvement. She failed to attend for some time and is now under treatment again without any hope of success.

Discussion.—A careful study of the clinical nature of the toxic effects of sulphonamides shows a close resemblance to the clinical manifestations of the deficiency of vitamin B₂ group and especially that of nicotinic acid.

Depletion of nicotinic acid in the body damages the very same four systems—the gastro-intestinal, circulatory, dermal and nervous—as sulpha drug poisoning does. The nature of the lesions of both is also similar, being degenerative rather than inflammatory in type. I have also noticed that sulpha drugs produce more toxic effects in a patient who already shows nicotinic acid deficiency and that the exhibition of nicotinic acid does act as a preventive and curative to the toxic effects of M&B 693 and other members of sulpha group. Our American colleagues are also using it in increasing number of cases with encouraging results. Moreover, there is experimental evidence that sulpha drugs interfere with vitamin B synthesis that takes place in the intestines of animals. If this intestinal synthesis also occurs in man (of which we have no definite proof as yet) sulpha drugs may be causing definite interference to the process and thus giving a severe depletion of vitamin B complex which may cause an enhancement of the toxic reactions of sulphonamides. The increased liability of neurosis, mental states, and other damage to the nervous system now reported on the ingestion of sulphaguanidine or succinylsulphathiazole may be due to this cause, as there is less absorption of these drugs from the gut and thus they have an increasing opportunity to interfere with the synthesis of vitamin

B complex in the intestine. However, it is evident through animal experimentations and human autopsies that sulpha drugs cause epithelial degeneration. It is, therefore, rational to believe that nicotinic acid which essentially nourishes epithelial tissues should be able to guard them against the destructive action of the drugs and restore them to normal if the damage has not proceeded to total destruction.

Summary

1. Two cases of optic atrophy with blindness due to M&B 693 are described.
2. The probable nature of the lesion in sulphonamide amblyopia and the rationale of its treatment with nicotinic acid are detailed.
3. Restoration of sight with nicotinic acid in one case and its failure in the other are recorded.

Acknowledgment

I have to thank Lieut.-Colonel F. E. R. Laborda, the Chief Medical Officer, East Indian Railway, for his permission to get the note published. I am indebted to Dr. M. U. Khan, Medical Officer in charge M. D. Eye Hospital, Allahabad, for the notes of the above two cases and for his special care and co-operation in noting the effects of nicotinic acid on the damaged nerves ophthalmoscopically and in other ways.

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TOLERANCE TO ENTEROVIOFORM TABLETS

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IN spite of the widespread and often indiscriminate use of enterovioform tablets there are very few case reports in the literature of enterovioform intolerance. In this country at least, enterovioform has rightly come to occupy a very prominent place in the armamentarium of the practitioner. In view of its immense popularity and widespread employment, it is indeed surprising that not a single case of fatal poisoning from enterovioform has ever been reported. Toxic symptoms have been noted with great rarity and have invariably been mild in nature.

The value of the drug enterovioform (or more correctly 'Vioform') was proved for the first time in the amœbiasis of monkeys by Anderson and Koch in 1931, but it is to David, Johnstone, Reed and Leake (1933) that we are really indebted for the introduction of this drug in the treatment of human amœbiasis.

Enterovioform, the active substance of which is iodochlorhydroxyquinoline, has been found

to be of value not only in amœbic dysentery and amœbiasis but also in a host of other common and uncommon ailments such as bacillary dysentery, enterocolitis, summer diarrhœa, fermentative and putrefactive dyspepsias and even balantidial infections, lambliasis and ascariasis.

The great majority of workers agree on the low toxicity of enterovioform.

It is said that the rabbit will tolerate quite easily one gramme of enterovioform per kilogram body-weight, given orally or rectally; even when two grammes per kilogram are administered daily for fourteen days, no toxic symptoms are perceptible. Rabbits receiving 250 mg. in a single dose have shown fatty infiltration of the liver as well as damage to the renal tubules (Craig, 1934).

In man, David, Johnstone, Reed and Leake (1933) observed no signs of toxicity or unusual symptoms in any of their forty-seven cases of amœbiasis. In 1931, Anderson and Reed noted toxic symptoms in three out of sixty cases of amœbiasis treated with enterovioform. In one case there were reported palpitation, dyspnœa, headache and sense of fullness in the head. In the other two cases, there were gastro-intestinal symptoms like colic, flatulence and diarrhœa.

Excellent results have been reported in acute and chronic amœbiasis by a host of authors (Azmy Bey and Taha, 1934; Giordano, 1934; Lopez Ramirez and Galan, 1935; Ugrankar, 1938) with no toxic symptoms whatsoever. Even when administered by El-Biblawi (1936) to two pregnant patients, enterovioform caused no side effects.

The extremely low toxicity of enterovioform commented on by numerous workers in the past, is confirmed in full by the amazing degree of tolerance exhibited by my patient to the protracted administration of enterovioform.

Case report

A Bori patient, aged 35, was brought to me for examination on 14th August, 1944, for symptoms suggestive of cardiovascular disorder. In June 1944, the patient started noticing a gradually increasing lassitude and excessive fatigue on walking or climbing stairs. This was followed by frequent headaches, mainly frontal in type, mental depression and dyspnœa on effort.

There were no pains in the chest and no disturbance of bowel movements. On enquiry, he gave a most interesting history. In the middle of 1943, he had been examined for intestinal pains, diarrhœa and mucus in the stools by a consulting physician in Bombay who had prescribed enterovioform tablets by mouth, six tablets a day. The patient being relieved of all his intestinal symptoms within a fortnight of its administration was tempted into continuing these tablets without a break until August 1944, i.e. for a period of eleven months, during which time he finished, in all, one hundred bottles of enterovioform or two thousand tablets!

On examination, he was found to be a thin, undernourished individual of morose disposition. He showed signs of excessive nervous irritability and displayed a fine tremor of the outstretched hands. There was no pallor or cyanosis, no œdema, engorgement of veins or

liver enlargement. The apex beat was in the fifth space, $3\frac{1}{2}$ inches from the mid-line, the cardiac boundaries were normal on percussion, the first sound at the apex was definitely reduced in intensity and 'muffled', the second sound appeared accentuated in the pulmonary area. No murmurs were audible. On fluoroscopy, there was neither dilatation of the aorta nor enlargement of the heart. The blood pressure was 104 mm. systolic and 70 mm. diastolic with a cardiac rate of 116 per minute. An electrocardiogram could not be obtained.

He was advised to take complete rest in bed for some weeks, to take a light diet and was given one digoxin tablet and one coramine tablet three times a day after meals for five days in every week. He was also given intravenous injections of 50 c.cm. 25 per cent glucose daily for about twelve days. After three weeks of treatment, he was re-examined and found to display no abnormal signs on examination. Besides being relieved of all his symptoms, the first sound of the heart was found to be of normal intensity and character, the blood pressure was 132/78 with a pulse rate of 70 per minute and the electrocardiogram taken at this time was normal in all respects.

Summary.—In the present case report, the following features are worthy of note:—

(1) Enterovioform tablets were taken by my patient continuously at the rate of six a day and with no breaks whatsoever for a period of over eleven months, making a total of 2,000 tablets.

(2) No symptoms or unpleasant side-effects were complained of until about nine months after the start of this course.

(3) The toxic symptoms complained of (and arising after the administration of over 1,500 tablets) were, comparatively speaking, mild; palpitation, dyspnoea on effort, undue fatigue, feelings of lassitude, depression and frontal headache were the only symptoms noted by the patient. On examination, I noted a weak or muffled first sounds at the apex, sinus tachycardia (116 per minute), and a low blood pressure (104/70).

(4) There was a rapid response to cardiotonic remedies, with complete disappearance of abnormal symptoms and signs within three weeks of treatment.

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A NEW MANIFESTATION OF ARIBOFLAVINOSIS

LESIONS OF THE VULVA

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Case report

A PARSEE girl, aged 18, was treated last year for typhoid fever. She ran a continuous fever ranging from 99°F. to 106°F. for a period of about two months before succumbing finally to a toxic myocarditis and intestinal hæmorrhage. It was during the fifth week of fever that she presented symptoms and signs of a vitamin deficiency. She started complaining of a 'raw feeling' in the mouth, soreness of the tongue and difficulty in swallowing.

On examination, there was abnormal redness with slight crusting of the lips, especially at the angles of the mouth. The tongue was dark red, raw and angry-looking, with a tendency to fissuring along the sides. The fauces were mildly infected and flushed.

In addition to these symptoms, there was complaint of 'burning' sensations and discharge in the region of the vulva. On examination, a light yellow mucus discharge was seen over the vulva, which appeared congested and raw. Both the orifices, urethral and vaginal, showed red 'haloes' around them.

Because of her mouth lesions, she was put on riboflavin tablets (Lilly), each tablet containing 1 mg. riboflavin equivalent to four hundred Sherman units of vitamin B₂ (g.) (1,000 gamma of riboflavin). She was given riboflavin at the rate of six tablets a day. Within three days of starting this treatment, there was a rapid amelioration of symptoms and signs and within six days of treatment, the oral and vulval lesions had disappeared completely.

Discussion

Though lesions of the tongue and lips have been reported on numerous occasions in riboflavin deficiency, vulval lesions do not appear to have attracted the attention of workers so far. In a search of the literature, I could find no allusion to any such lesions of the vulva in cases of ariboflavinosis.

In the case reported here, the vulval lesions have been attributed to deficiency of riboflavin for the following reasons:—

1. The simultaneous appearance of oral and vulval lesions, the oral lesions being typical of riboflavin deficiency.

2. The rapid and simultaneous disappearance of both lesions, oral and vulval, on riboflavin treatment.

3. Disappearance of the vulval lesions, in the absence of all other treatment, oral and regional.

Summary

A case is reported of typhoid fever with symptoms and signs of ariboflavinosis developing during the fifth week of the disease. In addition to the typical oral lesions of ariboflavinosis, there were atypical 'vulval lesions' which have not been described so far in this form of deficiency disease. The oral and vulval lesions after appearing simultaneously responded promptly to riboflavin therapy.

SOME BIOCHEMICAL NORMALS IN BENGALIS*

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THE quantitative determination of the biochemical constituents of blood in normal Bengalis and the establishment of normals for Bengalis are necessary to evaluate findings after such examination of blood and other body fluids in case of diseases for both diagnosis and prognosis. The normal standards used at present for comparison are those for Europeans and Americans as studied by Ponder (1922), Folin and Svedberg (1930); Danielson (1933, 1936), and Wu (1922), and those for the people of the Bombay presidency by Gokhale (1939). Since dietetic variations and climatic conditions (Wright, 1940; Bodansky, 1938; Peters and van Slyke, 1931) are known to exert some influence on the biochemical constituents of blood, it is not desirable to compare figures for Bengalis with those of others who differ from them in details of diet and also in their environmental conditions. It has therefore been considered necessary to examine the biochemical constituents of blood of the Bengalis and thereby arrive, if possible, at a normal or standard figure for the Bengalis.

Subjects examined

One hundred and thirty-one male persons have been examined. They were all healthy Bengalis, most of whom were medical students and junior men of the profession, their age varying from 20 to 30. Their diet is a mixed diet containing invariably some animal protein, principally fish. In majority of these cases milk and tea and in some cases coffee form a part of their breakfast.

Methods

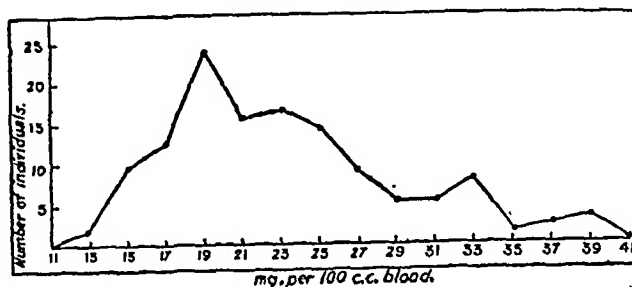
Urea, non-protein nitrogen (in fact 'non-colloid' nitrogen), uric acid, preformed creatinine, chloride and cholesterol have been determined by different methods, a brief description of which is given below:—

Blood was collected from the antecubital vein, mostly before meals and in a few cases immediately after meal and before the meal can exert any influence on the blood constituents. Neutral potassium oxalate (Merck) was used as anticoagulant to the extent of 2 mg. per c.c.m. of blood. Fresh and laked blood has always been examined and experiments repeated, whenever any suspicion, however slight, arose. Reagents used were of analytical quality and the experimental conditions were kept constant throughout. Hellige's colorimeter has been used for comparison.

Blood urea.—This was estimated by the method of van Slyke and Cullen (Peters and van Slyke, 1931). Urea in the blood is hydrolysed to ammonium carbonate by the action of the enzyme urease in the presence of a phosphate buffer (Peters and van Slyke, 1931) which

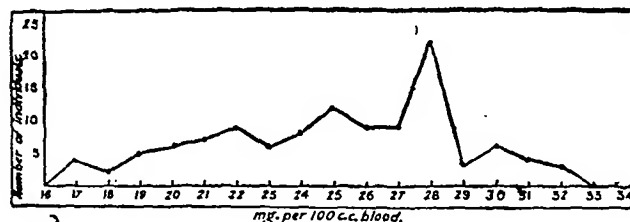
maintains suitable reaction during enzyme action. Ammonia is then driven off on addition of potassium carbonate by a current of air. This ammonia is received in a cylinder containing a measured quantity of acid. After aeration for about an hour by a good current

Graph 1. Urea.



of air, the acid in the cylinder is titrated with known alkali using phenolphthalein as the indicator instead of methyl red. In this way the amount of nitrogen derived from urea contained in the amount of blood taken is estimated from which urea figure is deduced per 100 c.c.m. of blood.

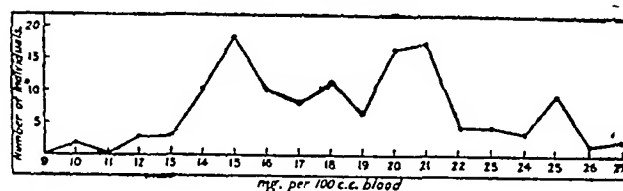
Graph 2. Non-protein nitrogen.



Non-protein nitrogen.—Trichloroacetic acid filtrate is used. Nitrogen is determined in this filtrate. The filtrate is digested by micro-kjeldahl method. A few glass beads are added during digestion to prevent bumping. When the digestion mixture is crystal clear, it is aerated after addition of sufficient caustic soda in place of potassium carbonate as in the estimation of urea. Ammonia that evolves, is received in acidulated water. This is titrated with known alkali using phenolphthalein as the indicator, wherefrom non-protein nitrogen value is estimated.

During the process of aeration of both urea and non-protein nitrogen ammonia from the atmospheric air has been arrested in an acid tube prior to its entry into the tube containing either the blood or the digestion mixture. The writer was conscious of the probability of errors from other sources during experiments, namely, sulphuric acid, urease water, potassium carbo-

Graph 3. Creatinine.



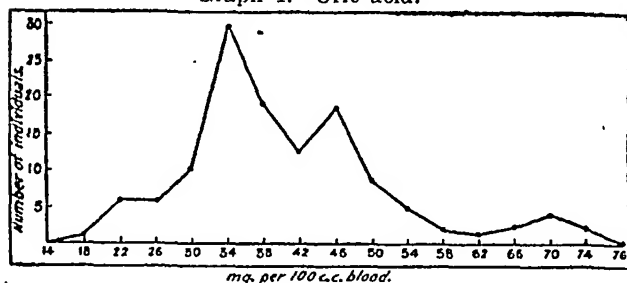
nate, potency of acids and alkalies, etc., and avoided them as far as practicable. The potency of urease powder to break down urea has been tested before any new brand has been used in the actual hydrolysis.

Creatinine (preformed).—Folin's filtrate (of laked blood) is treated with freshly prepared alkaline picrate and the colour thus developed is compared with a known standard in a colorimeter.

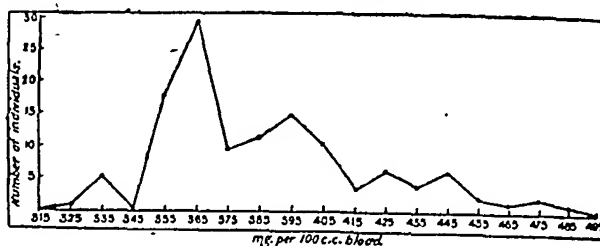
Uric acid.—Folin's filtrate (tungstic acid filtrate) of laked blood is treated with specially prepared sensitive uric acid reagent (Harrison, 1937) and the colour is developed with 15 per cent sodium cyanide solution.

* Condensed by the editor.

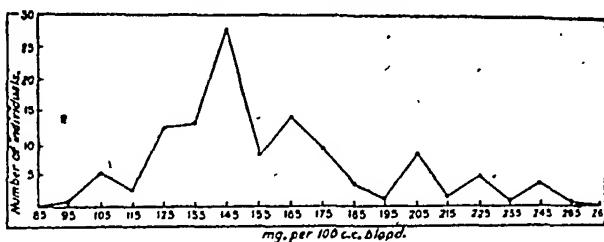
Graph 4. Uric acid.



Graph 5. Chloride.



Graph 6. Cholesterol.



Uric acid is then determined in the blood colorimetrically [for details in method *vide* Harrison (1937)].

Chloride.—Van Slyke and Sendroy (Peters and van Slyke, 1931)—chlorides are precipitated from blood, proteins are oxidized by heating with concentrated nitric acid in the presence of silver nitrate. The excess of silver is titrated with thiocyanate solution using ferric ammonium sulphate as an indicator as in Whitehorn's method (1921).

Cholesterol.—Bloor (1928) modified—lipoids are extracted with a mixture of hot alcohol and ether. The mixture is filtered and the filtrate is evaporated to dryness and the cholesterol is extracted with chloroform. In this extract acetic anhydride colour reaction is developed with acetic acid anhydride and sulphuric acid. The cholesterol is then determined quantitatively in the colorimeter.

The results obtained in this study are summarized in table I:—

These results are plotted in graphs 1 to 6 which bring out their significance clearly.

The results obtained by various workers for the respective biochemical constituents as compared with those obtained in the present investigation are tabulated in table II.

TABLE I

Average and range in the findings of healthy normal young Bengali males

	Number of persons examined	Mean in mg. per 100 c.cm.	Range in mg. in the values obtained	Standard deviation	Percentage of subjects within standard deviation	Number and percentage of individuals within the range of probable error*
Urea	131	22.23 \pm 0.34	12-38	5.85 \pm 0.24	74.8	82 (62.6)
N.P.N.	122	25.59 \pm 0.27	17-36	4.39 \pm 0.19	75.4	75 (61.4)
Creatinine (preformed) ..	127	1.85 \pm 0.023	1.0-2.7	0.38 \pm 0.02	80.3	86 (67.7)
Uric acid	127	4.04 \pm 0.07	1.8-7.2	1.14 \pm 0.05	80.3	85 (67.0)
Chloride	128	386.76 \pm 1.98	290-480	33.33 \pm 1.41	83.1	80 (62.5)
Cholesterol	119	158.95 \pm 2.18	100-250	35.43 \pm 1.55	75.1	75 (63.4)

*The range of probable error of the normal curve includes all individuals that fall within the limits of $0.6745 \times \sigma$ on either side of the mean. (*Vide* An Outline of Biometric Analysis, by Allan E. Treolar, 1936 edition, page 23.)

TABLE II

A few normal averages of biochemical constituents of laked blood as worked out by different authors in mg. per 100 c.cm.

	Urea	N.P.N.	Uric acid	Creatinine preformed	Cholesterol	Chloride
Folin and Svedberg ..	27.0	30.7	2.5	1.38
Hawk and Bergeim ..	21-32	25-35	2-3.5	1-2	140-180	450-500
Peters and van Slyke ..	18-38	25-40	2.5-5	1-2	100-230	..
Gokhale ..	27.8	30.4	3.02	1.17
Mukherji ..	24.0	27.4	4.6	1.08
Bloor <i>et al.</i>	167-255	..
Myers and Wardell	100-200	..
Present series (Chakrabarty) ..	22.3	25.6	4.0	1.8	158.9	386.7

Summary and conclusions

1. Figures are based on the examination of 131 healthy young Bengali males varying in age from 20 to 30 years.

2. Normals for several biochemical constituents of blood have been determined.

3. They have been compared with normals as determined by different authors in India and outside India.

4. The figures indicating different normals appear to be lower than those for non-Indians and also lower than those for the people of the Bombay presidency except the figures for uric acid and preformed creatinine which are higher.

Acknowledgment

My thanks are due to Rai Bahadur Dr. A. R. Majumdar, Superintendent, Campbell Medical School and Hospital, Calcutta, for his help in carrying out the work. I am grateful to Professors T. Roy Choudhury and M. N. Basu of the Calcutta University for the statistical portion. I also express my gratitude to Dr. B. Mukherji for encouragement in the completion of the paper.

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[The manuscript of the article contained a long table giving the details of all the estimations made in 131 persons. This table has been omitted to save space.—EDITOR, *I.M.G.*]

A Mirror of Hospital Practice

A CASE OF POST-CONCUSSIONAL HEADACHE*

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 Superintendent, Camp Jail, Govindpur,
 Manbhum District

In recent years, post-concussional headache and its disabling effects have frequently been stressed. The following case may be of interest :—

A young man had a motor-cycle accident, and he was found unconscious on the road with bleeding from the nose. There were small lacerated wounds on the right wrist, on the back of the left ear and above the eyebrow, with minor abrasions elsewhere. After a short time he recovered consciousness, and in the following days the wounds healed. There was apparently no injury to the skull but x-ray was not available. During the following days there was severe headache in the frontal and temporal regions of a throbbing nature. This gradually grew worse and was aggravated by sneezing and coughing. It was not relieved by analgesics. During the bouts of headache the temporal arteries were prominent and were seen to throb. The bouts of headache gradually increased in frequency and in intensity. Fifteen days after the accident a lumbar puncture was done and about 10 c.c.m. of clear fluid under increased pressure were withdrawn. The immediate effect was the disappearance of the headache. That evening however it returned slightly, but it did not recur again.

* Abridged by the editor.

A CASE OF TROPICAL EOSINOPHILIA DEVELOPING AGRANULOCYTIC ANGINA DURING ARSENICAL THERAPY

By R. N. CHAUDHURI, M.B. (Cal.), M.R.C.P. (Edin.),
 T.D.D. (Wales), F.S.M.F. (Bengal)

and

M. N. RAI CHAUDHURI, M.B. (Cal.)

(From the School of Tropical Medicine, Calcutta)

DURING 1944, we treated at the Carmichael Hospital for Tropical Diseases 14 patients suffering from tropical eosinophilia with organic arsenicals; of these nine were given intramuscular injections of acetylarsan at intervals of about five days, with satisfactory results, the course being uneventful except in one case which is reported here.

This patient developed sensitiveness to the drug and passed into an alarming state of agranulocytic angina.

Case report

The patient was an Indian woman, aged 22 years, admitted to a hospital on the 10th August, 1944, with a diagnosis of 'eosinophil lung'. The symptoms were chronic cough with slight expectoration, occasional asthmatic attacks, irregular low fever, indefinite pains in

the abdomen, progressive weakness and loss of weight; duration about one year. Except dysentery in childhood and epidemic dropsy at the age of 11, she had no illness of importance in the past. There was no history of any chest disease in the family.

On admission, her temperature was normal. Lungs—scattered expiratory rhonchi on both sides and a few râles on the right side of the chest. The liver was slightly enlarged but the spleen was not palpable. The heart was normal; blood pressure 96/65 mm. Hg. She had a leucorrhœal discharge with burning micturition at times. There was a movable kidney on the right side. Pelvic examination at the Eden Hospital revealed cystocele with enlarged tender ovaries. The total and differential counts are given in the table. The Wassermann reaction was negative and the blood sedimentation rate was 95 mm. in one hour (Westergren). The sputum showed no acid-fast bacilli on three consecutive examinations. The urine was clear, the culture being sterile. *Giardia intestinalis* was found in the stools in fair number. A skiagram of the chest showed diffuse mottling in both lung fields (see figure in plate IV) which is a common feature of tropical eosinophilia.

Treatment consisted of intramuscular injections of acetylarsan, 3 c.cm. at intervals of 5 days. No untoward effect was observed until the third injection, when the patient had a rise of temperature to 102°F. for 24 hours. The fourth injection was given as usual, after which

outstanding symptoms being high continued fever (maximum temperature 105°F.), toxæmia and extreme weakness. At this time she also started menstruating, rather profusely. *Streptococcus viridans* was isolated in throat culture.

A diagnosis of agranulocytic angina was made, but sodium pentose nucleotide not being available, the patient was given an intramuscular injection of crude liver extract (Lilly), 4 c.cm. and intravenous glucose, 50 c.cm. of 25 per cent solution, with vitamin C 100 mg. These injections were repeated daily, and on the third day of this treatment, the clinical condition of the patient seemed encouraging; the temperature came down to 100°F., the patch in the uvula cleared up, and she felt better. On the same day, a supply of pentnucleotide was received, and she was given 15 c.cm. intramuscularly, while the liver injection was stopped but the intravenous glucose with vitamin C was continued. As the patient's condition had considerably improved, pentnucleotide was however not repeated. The temperature became normal two days later, and the leucocyte count on 6th October was 8,500 with 69 per cent neutrophils, 21 per cent lymphocytes, 4 per cent monocytes and 6 per cent

Total and differential counts

Date	12-8-44	26-8-44	30-8-44	7-9-44	12-9-44	15-9-44	19-9-44	22-9-44
Hæmoglobin (in gm.) ..	9.6	9.3	9.6
Red cells (in million) ..	3.60	3.40	3.50
Leucocytes (in thousands)	21.5	25.0	17.2	10.0	8.0	6.0	4.4	7.6
Neutrophils, per cent ..	14	14	10	30	12	6	21	58.5
Lymphocytes, per cent	18	18	24	38	70	63	52	31.5
Monocytes, per cent ..	2	1	1.5	8	6	20	6	4
Eosinophils, per cent ..	66	67	64.5	24	12	11	21	6

(The total leucocytes and granulocytes in thousands are also represented in the temperature chart.)

the temperature rose to 100°F. but was normal next day. Since her general condition remained good, the cough was less and the blood picture was improving, it was decided to continue the treatment, and the fifth injection was given in due course. Again, there was rise of temperature to 102°F., and now she complained of pains in the body including the gums and throat, but no obvious abnormality was found locally. The temperature was irregular for three days and then became of continued type (see chart). A slightly raised respiratory rate and a few scattered rhonchi were the only chest findings. She also complained of frequent micturition. A catheter specimen of urine contained a trace of albumen and a few pus cells, but was sterile on culture. On the 7th day of the fever, there was an exacerbation of the throat pain, and deglutition became difficult. Examination now revealed a grey slough on the uvula with enlargement of the tonsillar and submental lymph nodes. The tongue was furred and dry, and she appeared very ill, the

eosinophils. Thereafter, the patient kept well with practically no cough. Another skiagram of her chest taken about this time, however, showed no change in the appearance of the lungs. She was discharged from the hospital on 27th October with a request to report later.

Discussion.—An unusual condition of granulocytopenia with faucial inflammation developing in a case of tropical eosinophilia during a course of acetylarsan injections is reported. The patient took the first two injections well, but thereafter became sensitive to the drug, as shown by febrile reactions after each subsequent injection, and the white cell count went down fairly rapidly. The reaction after the fifth one was a severe one; the patient was desperately ill with high fever, toxæmia and exhaustion of the leucoblastic tissue of the bone marrow, the neutrophils in the peripheral blood having been reduced to 6 per cent with a definite increase of monocytes, when a grey patch appeared in the throat with enlargement of the cervical lymph nodes.

INTRADIPLOIC EPIDERMOID OF THE SKULL :
B. N. BALKRISHNA RAO. PAGE 125.

A CASE OF TROPICAL EOSINOPHILIA, ETC. : R. N. CHAUDHURI AND M. N. RAI CHAUDHURI. PAGE 151.

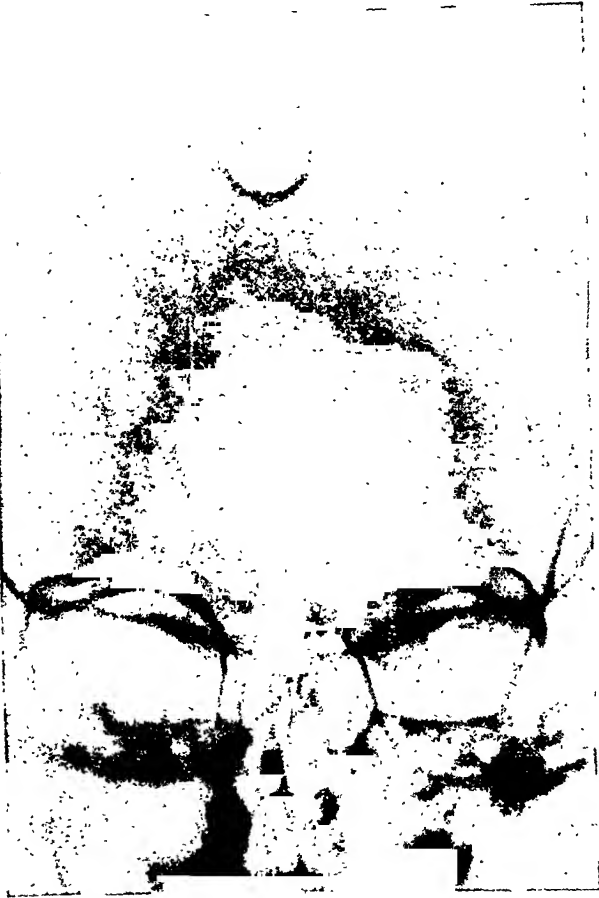
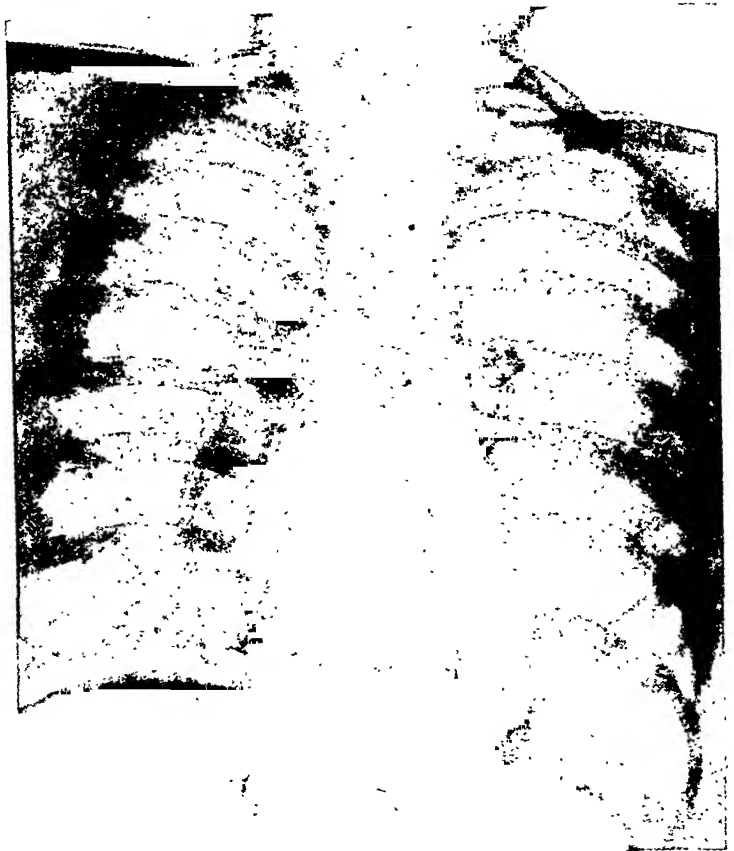


Fig. 1.—Skull showing circumscribed deficiency of both tables.



Diffuse mottling in both lung fields.

GNATHOSTOME INFECTION OF THE EYE :
A. K. MUKERJI & N. V. BHADURI. PAGE 126.

SOLITARY SPLENIC CYST : N. A. AIENGAR AND
V. R. NAIDU. PAGE 131.

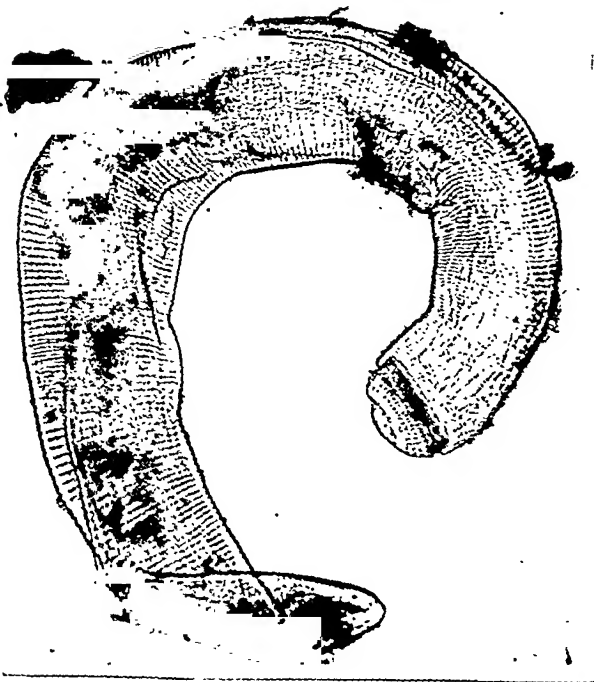


Fig. 1.—Photomicrograph of the worm with adherent bits of iris tissue.



Photograph showing the splenic cyst.



Fig. 1.—'Tropical ulcer', 5 inches by 5 inches, on the lateral aspect of the leg extending down to the foot, before treatment. Duration 4 months.

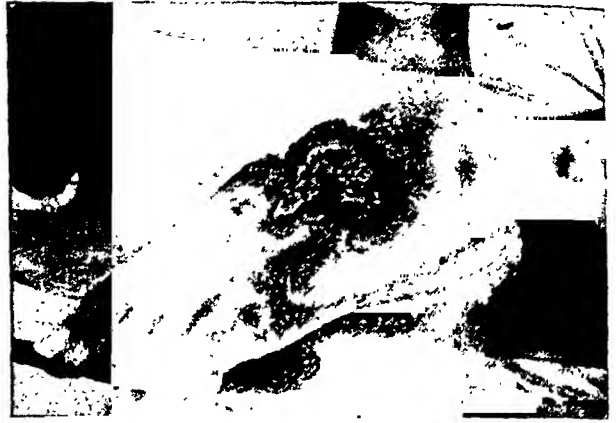


Fig. 4.—Healing ulcer on the dorsum of the foot, four weeks after the application of the sulphathiazole cod liver oil paste. The original ulcer was 3 inches by 3 inches, of three months' duration and resistant to treatment.

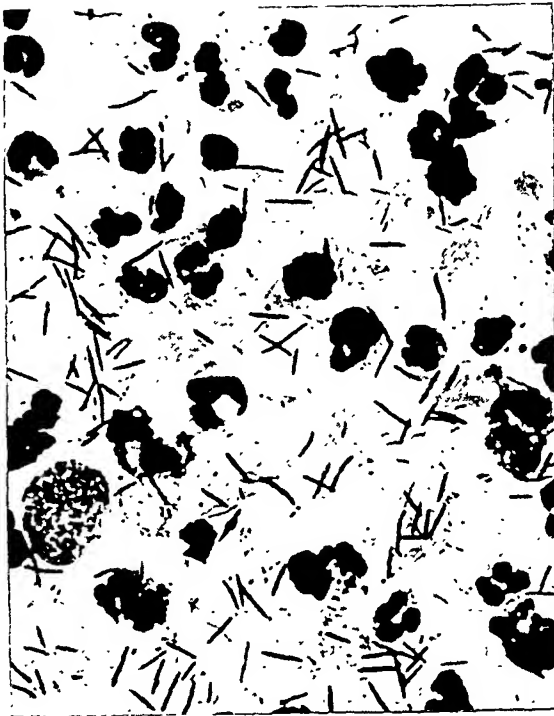


Fig. 2.



Fig. 3.

Figs. 2 and 3.—Photomicrographs of stained smears of the discharge from the ulcer showing fusiform bacilli and *Treponema vincenti* (× 970).

The treatment of such an acute condition usually includes discontinuance of the incriminating drug, pentnucleotide injections and possibly blood transfusion, while liver injections have been advocated especially for chronic neutropenia. As pentnucleotide was not available for 3 days, the patient was given injections of crude liver plus intravenous glucose with vitamin C. The clinical response was striking; the rapid downhill course was readily checked, and she began to show steady clinical improvement.

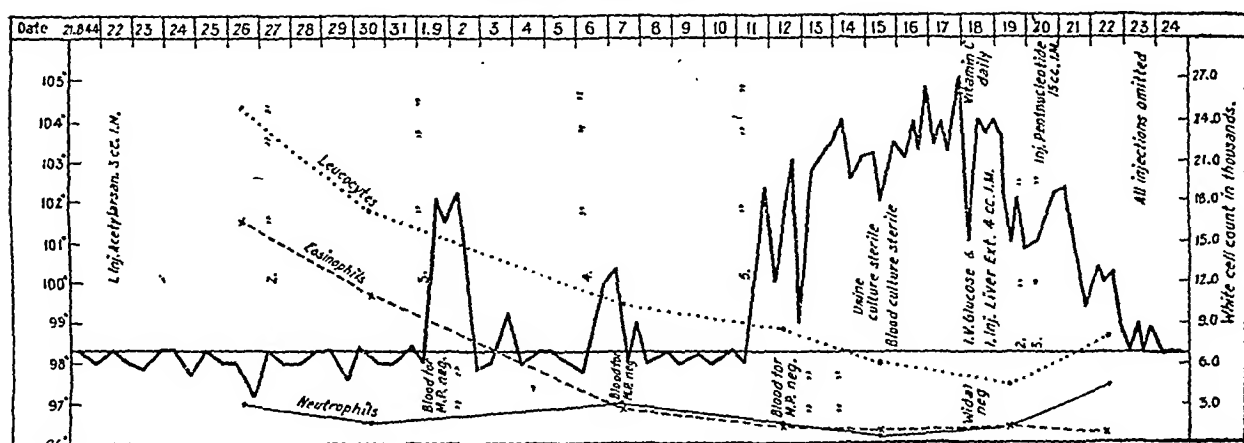
Although spontaneous recovery of agranulocytosis without any specific therapy has been reported, it seems that the above therapy was responsible for the rapid improvement in this

had she any history of slightest injury during pregnancy. She had had intermittent fever only two days previous to the date of delivery and it subsided by taking quinine orally. Unfortunately no blood slide was taken at that time. She was confined on 3rd August, 1944, and her child was attacked with fever on the 9th (6th day after delivery).

Condition on admission.—Temperature 103.6°F., pulse uncountable; the child was gasping. A blood slide was taken at once which showed M.T. rings. Quinine gr. 1 was administered by mouth and had no effect and the child died.

Comment.—The child had a rise of temperature on the 6th day after birth when M.T. rings

TEMPERATURE CHART



case, and the small quantity of pentnucleotide administered subsequently had probably little or no effect.

There is another interesting feature worth noting in this case, namely the mottling of the lungs persisting even after the blood picture became nearly normal. This suggests that it is not necessarily dependent on massive eosinophilia in the peripheral blood. Perhaps it takes much longer time to clear up than the blood condition, and it is also probable that a few more arsenic injections might have brought about the radiological improvement, but these were withheld for obvious reasons.

MALARIAL INFECTION IN THE NEW BORN

By SURJYA KUMAR BHOWMICK, L.M.F.
Assistant Medical Officer, Telepara Tea Estate,
Binnaguri P. O., Jalpaiguri

THE protective action of the placenta fails when there is any injury (during pregnancy) resulting in placental hæmorrhage [Clark (1915), Jean (1927) and Thonnard-Neumann (1931) and others]. Das Gupta (1939) thinks that the failure of the protective function is more probably due to prolonged parasitic invasion.

But in the following case the mother was neither suffering from chronic infection nor

were found in the peripheral blood. The incubation period of *Plasmodium falciparum* is nine to twelve days. So it can be concluded to be a case where congenital transmission occurred.

A CASE OF RETROPERITONEAL ABSCESS

By B. L. CHOPRA, L.R.C.P., L.R.C.S., L.R.F.P.S.,
D.P.H., D.T.M. (Eng.)

Divisional Medical Officer, N. W. Railway, Ferozepore

A SHED CLERK from Bahawalnagar was admitted on 29th May, 1944, with a diagnosis of retrocæcal appendicitis. On admission, he complained of the presence of a big mass in the right iliac region for about 20 days, with slight pain and tenderness on pressure. He also complained of dizziness on stretching the legs. He ran a remittent type of temperature, 99°F. in the morning and going up to 101°F. in the evening, of about the same duration. His bowels were constipated.

History of the present illness.—About 20 days before admission, he got pain of moderate severity in his epigastrium at 10 in the morning after his breakfast with a slight rise of temperature, but no vomiting. The pain persisted for three or four days. He had relief for a few days, and one day again there was high temperature, when he noticed a swelling in his right iliac region about the size of a walnut, which gradually increased to the present size. It was after a long consideration that he decided to undergo a long journey to this place as he knew of a friend of his who was cured after an operation.

On physical examination, the general condition of the patient was fair and the tongue was dry. Inspection

of the abdomen revealed a bulging in the right lumbar region especially when seen from the back. Palpation revealed a big ovoid mass extending from the right iliac and right lumbar region up to the right costal margin pointing more towards the lumbar region. It was hot to touch, and there was no redness or oedema of the skin over it. It was tender on pressure and did not move on respiration to any appreciable extent; firm and fairly hard in consistency. Fluctuation was present. Percussion produced a dull note. Rectal examination was made with a view to confirm the diagnosis of retrocaecal appendicitis, but no such sign could be elicited. Diagnosis of retroperitoneal abscess was, therefore, made after this examination.

Blood examination showed 25,000 white blood cells per c.mm. with 80 per cent polymorphs. Urine examination did not show anything abnormal.

Treatment.—Ordinary medical treatment was tried for a few days with sulphonamide and glycerine enema for obstinate constipation. Locally ichthylol-belladonna glycerine paint and antiphlogistine were applied.

Operation.—An incision, about 4 inches long, was made on the latero-posterior side under chloroform. Soon after cutting a few layers of muscles, pus gushed out; about one pint of stinking thick greenish pus was withdrawn. A rubber drainage tube was put in. After the operation, the temperature never went higher than 99°F., and it became normal four days after the operation. The white cell count came to 10,000 per c.mm. within two weeks. The drainage tube was reduced by half an inch daily, and on dressing very little discharge was noticed. The wound healed by first intention, leaving no scar. The dressing was done with cilazol powder. On 22nd July the man was discharged to duty.

My thanks are due to Dr. C. D. Newman for his permission to publish this case report.

TWO CASES OF ANTHRAX TREATED WITH SULPHANILAMIDE*

By D. K. PAUL, L.M.P.

Assistant Medical Officer, Lungla T.E.

Case 1.—A Kalwar girl, aged 3 years, was brought to the hospital on 2nd June, 1943, with a complaint of slight pain and swelling on the left cheek where a red pimple was found on examination. For the first three days these complaints increased, and the pustule acquired a red infiltrated base; the temperature rose from 97.8 to 99°F. and the pulse rate from 110 to 120. During these days, treatment consisted of alkaline mixture orally and local dressing with carbolic lotion and hot compress. On the fourth day the pustule developed a dark slough in the centre and a ring of vesicle round it; the whole face was swollen and red; the temperature was 102°F. and pulse 130. A smear showed anthrax bacilli.

Treatment with sulphanilamide was started on the 4th day; 0.5 gm. given as initial dose followed by two 0.25 gm. doses every 4 hours. The next day the patient was a little restless, and the temperature rose to 102.8°F. and pulse to 140. Four doses of sulphanilamide 0.25 gm. each were given for two days. All symptoms improved, redness and swelling subsided, and the smear showed no anthrax bacilli. The number of sulphanilamide doses was reduced to three on the fourth day; and the drug was continued in reduced amount for four days more. Total sulphanilamide given was 5.36 gm. Afterwards sulphanilamide powder was dusted over the ulcerated surface. The patient was discharged cured on 14th June, 1943.

Case 2.—A chamar man, aged 22 years, came to the hospital on the 11th February, 1944, with a small pustule and slight oedema around it on the dorsum of the right

hand, duration three days. The pustule and oedema increased for the next two days till the whole dorsum became red, and the oedema increased to the whole forearm; the temperature rose from 98.2 to 101°F. A smear from the pustule on the 13th showed anthrax bacilli.

For the first two days, an alkaline mixture was given orally, and the local part was dressed with carbolic lotion (1 in 40) and compress. On the 13th, 2 gm. of sulphanilamide was given followed by two 1 gm. doses every four hours; on the 14th three doses of 1 gm. each and on the 15th four doses of 5 gm. each were given. The temperature began to fall from the 15th till it was normal on the 17th. The drug was continued up to the 20th, three 0.5 gm. doses daily. The total amount of sulphanilamide given was 15 gm.

Conclusion

Though sulphanilamide has not taken any place in the specific treatment of anthrax, it can be said safely that it gives a good response in the treatment of anthrax. It is easy to get and administer while serum is not available everywhere and is more costly.

I express my thanks to Dr. N. N. Ghosh, Medical Officer, Lungla (Sylhet) Tea Co., Ltd., for his kind advice in the management of the cases and to Mr. E. W. Bishop, manager of the garden, for his help in dealing with them.

MASSIVE EPISTAXIS IN BENIGN TERTIAN MALARIA*

By P. N. LAHA, M.D. (Patna)

Lecturer in Diseases of Children, Medical College, Agra, U. P.

EPISTAXIS may be seen in many fevers besides malaria, and the amount of blood lost is usually small. In malaria, epistaxis may be seen but is usually not massive, and it is usually associated with *P. falciparum* infection. Its occurrence in *P. vivax* infection is rare.

Case report

A male child, aged 8 years, was admitted to hospital with a history of fever with rigor every day for four days and severe epistaxis for one day. About one pint of blood was lost at a time and one pint was lost after admission to hospital. There was no history of previous epistaxis or of injury.

The patient was acutely ill and intensely pale. There was slight icterus and the temperature was 103.6°F., pulse rate 124, respiration rate 24. The blood pressure was 76/50; the spleen and liver were enlarged 1 inch below the costal margin. The red cell count was 3,100,000, white cells 8,400, 60 per cent polymorphs; haemoglobin was 7.15 gm. A heavy infection of the blood with *P. vivax* trophozoites and gametocytes was found. *P. falciparum* was not seen. The platelet count was low. Examination of the nose showed one bleeding point in the anterior part of the septum.

Local cold application to the nose, and adrenaline plugs to the nose failed to control the bleeding. An intramuscular injection of 5 grains of quinine bihydrochloride was given, and two hours later the bleeding stopped. Subsequent treatment was with quinine given by mouth, and there was no further epistaxis.

The loss of two pints of blood was probably associated with thrombocytopenia occurring in severe malarial infection.

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Indian Medical Gazette

MARCH

PENICILLIN IN THE TREATMENT OF WOUNDS

In our last number we abstracted in an editorial the report of the Penicillin Clinical Trial Committee of the Medical Research Council on penicillin in the treatment of war wounds. This report gives a general account of the nature and the uses of penicillin, and forms the basis of our present-day knowledge of penicillin therapy, but its extensive use in the treatment of war wounds has made further advances possible, and these have been incorporated in a special issue of the *British Journal of Surgery* (1944, 32, 124) which contains a number of papers by various authors who have had considerable experience with the new remedy. In the Army it has been extensively used as a prophylactic against sepsis, and later, to control sepsis, but in the case of chronic sepsis, penicillin by itself is disappointing, but can be of value if allied to other procedures. The results in recent soft-tissue wounds are so good and the period of morbidity so lessened that they should be sutured with the aid of penicillin. The infected compound fracture is one of the most difficult problems that a surgeon has to face, while for the patients the illness is long and trying, and not infrequently ends in amputation or death. In an interim report of 70 cases of open fracture of the femur, the deaths and amputations were 1.4 and 2.8 per cent against 8.5 and 8.5 per cent of the control series. This is certainly an improvement, but penicillin failed to control sepsis fully. The mistakes and faults are being assessed and treatment is being modified in the light of the results so far obtained. In gas gangrene, radical surgery still remains the keystone of treatment, and no matter how much antiserum and penicillin are given, the outlook is gloomy indeed if radical extirpation is not possible; but there is no doubt of the value of the drug in checking the spread of the disease.

The meninges, pleura and the serous membranes of joints present a barrier across which penicillin does not readily pass. Infection in these sites should therefore be treated by local application, solutions of 1,000 to 2,000 units per c.cm. being used. It is a valuable aid to the treatment of infected hæmothorax, but as in the case of prophylactic treatment drainage may be required for the evacuation of blood clots and pus. It is also very useful in wounds of the head, but the methods of use are not yet standardized. Infective complications still arise because of the

difficulty of thoroughly cleaning the brain wound; it is often a narrow track extending deeply, and it requires gentle handling if uncontrollable hæmorrhage is to be avoided. Sulphadiazine is a useful additional agent in the prevention and treatment of meningitis, and should be administered where there is risk of infection of the cerebro-spinal pathways.

Finally, penicillin appears to be the most effective agent we have for treating gonorrhœa. In a series of 100 cases, 97 per cent responded successfully to one course of treatment, the drug being given intramuscularly in 20,000 units every 2 to 3 hours for 5 doses, up to 100,000 units. The average time that the patients came to hospital was the third day, and those that were hospitalized averaged 5.9 hospital days. Two per cent of the cases had epididymo-orchitis in which recovery was shortened. All the patients were later re-examined, when only 2 per cent were found to have active disease still. Good results were also obtained in sulphonamide-resistant gonorrhœa, 94.7 per cent being cured after one course of treatment, and the remaining requiring a second and, in very few, a third course.

In a series of 15 patients with early syphilis, penicillin was tried with total doses varying from 500,000 to 1,000,000 units given by 4-hourly injections during a period of 4 to 8 days. Two patients had febrile Herxheimer reaction which however did not interfere with the continuance of treatment. In all but one, spirochætes were not recoverable 14 hours after treatment was begun. The lesions healed in 3 to 7 days but the adenopathy subsided slowly. In 12 cases, the Kahn test became negative in 2 to 10 weeks after treatment. Further studies are required to find out whether these effects are permanent. In the meantime a warning is necessary. Penicillin is the only drug which is highly effective against both syphilis and gonorrhœa, but the dosage is different. Mention may be made of two patients in whom the treatment of gonorrhœa with 100,000 units apparently suppressed a coincident syphilitic infection with delay in the appearance of secondary lesions. Examination of a patient with gonorrhœa should include a careful search for lesions of early syphilis.

Certain fundamental principles must be observed if penicillin therapy is to be a success. There is a risk that excessive confidence in it may breed surgical neglect. After intramuscular injections, maximum concentration is reached in the blood within 15 minutes (hence intravenous injection has no special advantage), and excretion in the urine begins as soon as penicillin reaches the blood stream. In the fourth hour after a dose of 15,000 units, a bacteriostatic concentration, as a rule, no longer exists in the blood, so that the dose should be repeated 3 hourly. To avoid repeated injections, a continuous intramuscular drip is a very convenient method of systemic administration.

For local use, a continuous concentration of the drug must be maintained in contact with all infected tissues; one or two applications cannot be expected to remove the infecting organisms. Infection can easily flare up again if the treatment is cut short. It is better to err on the other side, and overdose is a good fault, though the surgeon should guard against the tendency to go on giving penicillin hopelessly for a long period instead of making a full surgical re-assessment of the case. The fact that the drug is innocuous to the patient may lead to careless use. Irrigation of an open wound is wasteful and ineffective. It is important to obtain full hæmostasis in order that the powder, when used, is not washed away by blood while the suture is proceeding. Local applications should be preferred whenever possible; it is much more economical, and patients much prefer it to the 3-hourly intramuscular injections. As previously stated, penicillin is incompatible with antiseptics, hence, before application, wounds should be cleaned only by soap and water or Catavlon. In the systemic treatment of early or localized infections, a course lasting 3 to 5 days may be enough, but for severe infection, treatment should be continued for at least 2 to 5 days after the infecting organisms can no longer be found by bacteriological methods. In a condition such as staphylococcal septicæmia, the total period of treatment is seldom less than 10 days. The general condition of the patient is a good guide to progress. Spirits and appetite improve, and local pain and swelling are relieved. The temperature often falls by lysis. In local treatment, pain is very quickly relieved and swelling disappears early.

Penicillin will prove to be virtually non-toxic, but impurities which accompany it at present sometimes give rise to minor reactions. Thrombophlebitis near the site of injection may develop after a few days of continuous treatment, but no serious results have been reported. A general urticaria may also occur. Treatment may however be continued and further courses safely given. A rigor may appear after intravenous administration; this may be due to penicillin or to the water or saline in which it is given.

Finally there should be no failure if penicillin is so applied as to be continually in contact with all infecting organisms in a bacteriostatic concentration.

Possible causes of failure are :—

- (1) Too small a dose or two infrequent application.
- (2) Dead tissue such as slough or sequestrum is present and is forming a focus of infection.
- (3) An infected area is not being reached by the drug. Such an area is formed by a large or thick-walled abscess, an infected serous cavity, sinuses, etc.
- (4) The bacteria are not susceptible.

(5) The penicillin preparation has lost its potency.

R. N. C.

SYNTHESIS OF VITAMINS IN THE HUMAN GUT

In a recent editorial (*I. M. G.*, Vol. LXXIX, p. 376), we discussed the paper of Najjar and Holt who reported for the first time the biosynthesis in the human gut of vitamin B₁. More information on the subject is now coming to hand, and it appears to be one of growing importance. We therefore refer to the subject again. The idea that vitamins could be synthesized in the gut was suggested about 30 years ago, and the occurrence of it in the gut of animals was first demonstrated 20 years ago. The production of vitamins in the gut of animals has been attributed to the presence of various micro-organisms in the gut. Vitamin production in the gut is apparently particularly marked in ruminant animals, whose rumen is naturally rich in micro-organisms including cellulose-splitting bacteria. During recent years, opportunity for further study of bacterial activity in the gut and vitamin production has been afforded by the discovery of the action of certain poorly absorbed sulphonamides, such as sulphaguanidine and succinyl sulphathiazole, in reducing or temporarily eliminating bacterial activity in the gut. The action of these sulphonamides in animals has been followed by a marked fall in the excretion of various vitamins, and this is attributed to interference with bacterial activity producing them. Practically all the known fractions of vitamin B have been shown to be synthesized in the gut of animals, and moreover it has been found that the amount of vitamin production in the gut is greatly influenced by diet. Numerous papers on this subject have appeared particularly in America during the last few years.

As recorded in our previous editorial note, these methods were first applied to man by Najjar and Holt in the U.S., who produced very strong evidence that vitamin B₁ is synthesized in the human gut. Since then, Najjar together with various other workers have produced similar evidence regarding the production of riboflavin in the human gut. In England similar lines of work have been pursued, and a report by Ellinger, Coulson and Benesch now appears recording the biosynthesis of nicotinamide. The *Lancet* discussing these matters in an editorial states that 'a striking fact is the enormous variation in the extent of biosynthesis in different people, even on the same diet, varying from 0 to 100 per cent of the requirement'. It is pointed out that these results may revolutionize our outlook on vitamins and deficiencies. Various observations suggest that it may be as important to have a diet encouraging vitamin B synthesis in the bowel as to

have a diet containing large amounts of vitamin B, and the question arises whether the use of sulphonamides in treatment of various conditions may not sometimes precipitate deficiency of vitamin B₁; not only will they prevent biosynthesis during the period of their administration but even when they have been stopped; and when the bacterial flora of the gut appear to have returned to normal, biosynthesis may be restored slowly, and it is suggested that the bacteria may have lost their power of synthesizing vitamins. Further developments of this line of work will be watched with interest, and it may have a considerable importance in this country. Is it possible that the relative rarity

of vitamin B deficiency in this country may be partly attributable to the fact that the predominantly vegetarian and rice diet, even if polished and deficient in vitamin B₁, together with the intestinal flora, may encourage the biosynthesis of vitamin B₁ in the gut? As we stated before in our previous editorial, it is difficult or impossible to correlate the distribution of beri-beri in Asia directly with diet, for it is much commoner in some countries in Asia in which the diet in some respects would appear to be better than in India where however the disease is rare.

J. L.

Medical News

MISSIONARY MEDICAL COLLEGE FOR WOMEN, VELLORE

THE Missionary Medical School for Women, Vellore (South India), is being converted into a Medical College teaching for the M.B.B.S. of the University of Madras and has been provisionally recognized for the first two years. The University Commission expects to visit the college in October 1945 with a view to full recognition. Moreover, it is planned to make it a college for men as well as for women. The appointments include the following: R. G. Cochrane, M.D. (Glas.), M.R.C.P. (Lond.), D.T.M. & H., as Principal. E. W. Gault, M.D., M.S. (Melb.), F.R.C.S., as Professor of Pathology. Draper, F.R.C.P. (Edin.), as Professor of Pharmacology. S. Carman, M.D., F.R.C.S. (Cantab.), as Professor of Surgery. Jameson, M.D., F.R.C.S., as Professor of Obstetrics and Gynaecology.

THE INDIAN HONOURS LIST

1ST JANUARY, 1945

THE following are the names of medical men, and others associated with medical institutions, in the Indian Honours List of date 1st January, 1945. We offer them our congratulations.

C.S.I.

Major-General J. S. S. Martin, K.H.S., I.M.S., Deputy Director of Medical Services, Central Command, India.

C.I.E.

Major-General W. C. Paton, M.C., I.M.S., Surgeon-General with the Government of Bengal.

F. C. Minett, Esq., M.B.E., Director, Imperial Veterinary Research Institute, Izatnagar-Mukteswar.

Lieutenant-Colonel (Local Brigadier) D. M. Fraser, I.M.S., Inspector of Medical Services, General Headquarters, India.

Rai Bahadur T. N. Banarji, Principal, Prince of Wales Medical College, Patna, Bihar.

O.B.E.

Miss Wenefrede Thompson, M.B.E., Lady Doctor, St. Luke's Mission Hospital, Lakhimpur, Dibrugarh, Assam.

Lieutenant-Colonel K. S. Fitch, I.M.S., Deputy Surgeon-General, Famine Relief, Bengal.

Captain T. J. Hurley, Director of Veterinary Services, Madras.

Major A. A. Pullar, I.M.S., Presidency Surgeon, Bombay.

M.B.E.

B. J. S. Bedi, Esq., Secretary, North-West Frontier Provincial Branch, Indian Red Cross Society, Peshawar.

S. S. Kundu, Esq., Officiating Civil Surgeon, Manipur State, Assam.

Kaisar-i-Hind Gold Medal

P. V. Benjamin, Esq., Medical Superintendent, Union Mission Tuberculosis Sanatorium, Arogyavaram, and Technical Adviser to the Tuberculosis Association of India, Chittoor District, Madras.

N. Macpherson, Esq., Surgeon, United Mission Hospital, Vellore, and lately Doctor-in-charge, Afghan Mission Hospital, Peshawar, North-West Frontier Province.

Colonel H. E. Shortt, C.I.E., I.M.S., Inspector-General of Civil Hospitals, Shillong, Assam.

Lieutenant-Colonel F. T. Simpson, M.C., lately Medical Officer in the Coalfields, Bihar.

Kaisar-i-Hind Silver Medal

Miss Lilian Aratoon, W.M.S., Lady Doctor-in-charge, Dufferin Hospital, Karachi, Sind.

Miss Vera Boyd, Matron, Civil Nursing Unit, Indian Military Hospital, Mhow, Central India.

Miss Amy Katherine Bullock, Matron, Welsh Mission Hospital, Shillong, Assam.

Mrs. Maude Currie, Voluntary Worker, Indian Military Hospital, Delhi Cantonments.

Mrs. Helen Doris Fox, Matron, Ranchi European Mental Hospital, Bihar.

Mrs. Alice Headwards, Surgeon-in-charge of the City Nursing Division, St. John's Ambulance, Bengal.

Mrs. Ethel Maude O'Neill, Matron, Government Women and Children Hospital, Madras.

Miss Violet Alice Quilley, Medical Practitioner, S. P. G. Mission, Ahmednagar, Bombay.

Miss Gwyneth Parul Roberts, Lady Doctor-in-charge, Welsh Mission Hospital, Durtlong, Lushai Hills, Assam.

Hiralal, Esq., First Assistant to the Doctor-in-charge of the Mungeli Christian Hospital, Mungeli, Bilaspur District, Central Provinces and Berar.

Bar to the Kaisar-i-Hind Silver Medal

Mrs. Ada Frances Morgan, Matron, Indian Hospital, Bengal-Nagpur Railway, Kharapur.

Kaisar-i-Hind Bronze Medal

Mrs. Ellen Gertrude Campbell, Sister-in-charge, Blood Bank, Calcutta, Bengal.

Mrs. Irma Heape, Lady District Superintendent, St. John's Ambulance Nursing Division, Bengal.

Motikala Magarni, Esq., Midwife and Nurse, Family Welfare Centre, 8th Gurkha Rifles Regimental Centre.

Mrs. Vijaylaxmi Oza, Red Cross Centre, Rajkot Civil Station.

Mrs. Alexander Maud Thompson, Lady Superintendent, St. John's Ambulance Brigade, Trichinopoly Cantonment, Madras.

A. C. Bhattacharjee, Esq., Assistant Health Officer, Siliguri, Bengal.

K. L. Malshet, Esq., Epidemic Medical Officer, Bijapur District, Bombay.

M. Masih, Esq., Medical Superintendent, Leper Asylum, Almora, United Provinces.

M. K. Sahib, Esq., Sub-Assistant Surgeon, Government Hospital, Tiruppattur, North Arcot District, Madras.

Khan Bahadur

Khan Sahib Abdul Majed, Deputy Surgeon-General, Calcutta, Bengal.

M. E. Merchant, Esq., Medical Officer, Bombay, Baroda and Central India Railway, Bombay.

Rai Bahadur

H. K. Dikshit, Esq., Civil Surgeon, Moradabad, United Provinces.

Rai Sahib U. M. Gupta, Professor of Pathology, Prince of Wales Medical College, Patna, Bihar.

Rai Sahib K. Misra, Civil Surgeon, Puri, Orissa.

Rai Sahib Dr. S. N. Malhotra, Chief Medical Officer and Sanitary Commissioner, Karauli State, Rajputana.

Rai Sahib L. S. Narain, Assistant Surgeon, Victoria Hospital, Ajmer.

Rai Sahib B. T. Kazi, Sub-Assistant Surgeon, In-charge, British Mission Hospital, Lhasa.

Rao Bahadur

Captain S. Thambayya, Additional Professor of Medicine, and Lecturer in Dermatology, Medical College, and Physician, General Hospital, Madras.

Sardar Sahib

Sardar B. Singh, Assistant Research Officer, Biological Products Section, Imperial Veterinary Research Institute, Izatnagar, United Provinces.

Khan Sahib

M. R. E. Siddiqi, Esq., Medical Officer-in-charge, Sadar Hospital, Bara Banki, United Provinces.

Qazi M. Said, District Medical Officer of Health, Ambala, Punjab.

Z. Hussain, Esq., Head Veterinary Inspector, Army Remount Department, Chenab Area, Lyallpur.

Rai Sahib

J. P. Varma, Esq., District Medical Officer of Health, Cawnpore, United Provinces.

D. Nath, Esq., Medical Officer (Retired), in Senior Sub-Charge, Ursula Horseman Memorial Hospital, Cawnpore, United Provinces.

D. Ram, Esq., Professor of Ophthalmology and Oto-Rhino-Laryngology (Officiating), Prince of Wales Medical College, Patna, Bihar.

M. Dave, Esq., Assistant Surgeon, Bhandara, Central Provinces and Berar.

Rao Sahib

A. Achyutan, Esq., Assistant District Medical Officer, Ootacamund, The Nilgiris, Madras.

S. Kalat, Esq., Private Medical Practitioner, Pollachi, Coimbatore District, Madras.

C. M. Mehta, Esq., Medical Practitioner, Kopergaon, Ahmednagar District, Bombay.

G. P. Phadke, Esq., Health Officer, Pandharpur Municipality, Sholapur District, Bombay.

P. J. Chandy, Esq., Medical Officer-in-charge, Leper Home, Fyzabad, United Provinces.

V. Massillamoney, Esq., Sub-Assistant Surgeon, Civil Medical Department, Government of Burma.

S. H. Padhye, Esq., Assistant Surgeon, Great Indian Peninsula Railway, Manmad.

O.B.I.

To the First Class with the title of 'Sardar Bahadur'

Indian Army Medical Corps

Subedar-Major Dharendra Nath Das Gupta, *Bahadur*, O.B.I.

Subedar-Major Muhammad Said Khan, *Bahadur*, O.B.I.

Subedar Jogendra Nath Khan, *Bahadur*, O.B.I.

Subedar-Major Buta Mall, *Bahadur*, O.B.I.

Subedar Pritam Singh, *Bahadur*, O.B.I.

Subedar Prem Roy Parsuram Pandya, *Bahadur*, O.B.I.

Subedar-Major Sardar Sahib Sapuran Singh, *Bahadur*, O.B.I.

Subedar-Major Dhari Ram Bhatia, *Bahadur*, O.B.I.

To the Second Class with the title of 'Bahadur'

Indian Army Medical Corps

Subedar Atar Singh Chatwal.

Subedar-Major Kanshi Ram.

Subedar-Major Albert Victor Dalip Singh.

Subedar-Major Hari Ram Parasar.

Subedar-Major Bakhtawar Singh.

Subedar Dharmanand Pandey.

Subedar Kumer Das.

Subedar-Major Muhammad Ramzan.

REPORT ON 'AMELLIN'

We have received the report on a trial of Amellin, carried out at the School of Tropical Medicine, Calcutta, by Dr. J. P. Bose, and by Dr. J. C. Gupta. Amellin is claimed to have anti-diabetic principles, and was tested at the request of the Director, Scientific and Industrial Research, Delhi, and the Secretary, Scientific Advisory Board, Indian Research Fund Association, Delhi.

The drug was supplied by Dr. M. C. Nath of Dacca. The first trial commenced from 7th August, 1944, the experiment being carried out strictly according to the instructions laid down by Dr. Nath. The patient was put on a diet consisting of 120 gm. of carbohydrate, 100 gm. of protein and 120 gm. of fat. The total quantity of urine and the total output of sugar in 24 hours was measured daily; weekly examinations of blood sugar were done all through the period of observation, i.e. for about 10 to 12 days, before the drug was started, during the experimental period and also afterwards.

The second trial of Amellin commenced from 8th November, 1944. This patient was having a diet consisting of 200 gm. of carbohydrate, 100 gm. of protein and 150 gm. of fat. At the commencement of the experiment his blood sugar was found to be 0.250 per cent and his total urinary sugar excretion in 24 hours was 79 gm. Amellin was administered strictly according to the direction laid down by Dr. Nath.

The results in the above two experiments are as follows: there was no marked difference in the urinary output of sugar. The blood sugar level at the

end of the experiment showed no change in the first patient, and was higher in the second patient. The weight of the first patient remained practically the same, and that of the second patient went steadily down; in the second patient, the general condition deteriorated markedly during this short period of observation and developed slight acidosis towards the end.

The drug was also found to be pharmacologically inactive in doses of 5 mg. and 10 mg. on cats weighing between 2 and 2½ kilograms. The active ingredient supplied was not sufficient to carry out any experiment to work out its action on metabolism.

NOTE ON THE J.S.B. METHOD OF STAINING MALARIA PARASITES

THE J.S.B. method of staining blood for malaria parasites was published in our March 1944 issue, page 102. A little time ago we received from the Malaria Institute of India a modification of the method of preparing the blue stain.

Increase the quantity five times as follows:—

Medicinal methylene blue	..	500 c.cm.
Potassium dichromate	..	0.5 gm.
1 per cent H ₂ SO ₄	..	0.5 gm.
Water	..	50 minims

Dissolve the methylene blue thoroughly in 500 c.cm. water. Add 1 per cent H₂SO₄, mix thoroughly and then add the chrome salt. A heavy amorphous purple coloured precipitate of methylene blue chromate forms. Heat in an autoclave at a temperature of 100 to 109°C. and a pressure of 0.5 lb. for 3 hours. At the end of this period, the solution turns blue which indicates almost complete polychroming. If the colour remains greenish further heating for another hour or so is required. If the temperature is allowed to rise above 110°C. the oxidation of methylene blue may be carried too far and the solution will turn violet purple.

When the solution has turned deep blue after 3 hours boiling, allow it to cool at room temperature. Then add 10 c.cm. of 1 per cent KOH or NaOH solution, drop by drop very gradually while constantly shaking the flask. After the total amount of alkali has been added, transfer half of the contents of the flask into another of the same capacity and continue shaking for 15 minutes more. Transfer the contents of the flasks into each other. In this way the precipitate will gradually get dissolved and the solution will turn deep blue with a violet iridescence. Leave it at room temperature for 48 hours for the solution to mature; afterwards filter through a soft filter paper. Delta brand no. 380 filter paper manufactured by Messrs. Delta Papier and Filter G.M.B.H. Duren Rl. serves the purpose. The solution will improve in staining properties with use and age.

We have also received the following note from Captain D. H. Robertson, I.M.S./I.A.M.C., from an Indian Field Laboratory.

The method of preparation of the J.S.B. stain, solution I, as described on page 103 of the *Indian Medical Gazette*, dated March 1944, has been slightly altered in that the mixture after the addition of the chrome salt and boiling for 3 hours is filtered through a fairly fine filter paper such as Whatman's no. 4. The filter paper, after filtration is complete, is placed in an incubator till thoroughly dry. The dried precipitate is then scraped off the filter paper into a clean mortar and ground up with a 1 per cent solution of potassium hydroxide, approximately 3 c.cm., this effects complete solution. Tap or distilled water is added to make up to 100 c.cm. Solution I is now ready for use.

The method of staining is the same as described by J.S.B.

INDIAN HEALTH GAZETTE,

No. 1, October 1944

We have received the first copy of the *Indian Health Gazette*, a new periodical, issued by the Government of India for circulation of news relating to health administration. It contains a number of articles, the first of which is a brief review of health conditions in India in 1943 when there was a high mortality from cholera, smallpox and 'fevers', the area most affected being Bengal. In this connection comment is made on the collections and reporting of vital statistics in this country which is far from accurate owing to lack of professionally trained staff, especially in rural areas. Attention is also drawn to the decline in the birth rate during the year; the biggest decline was recorded in Bengal and Behar with Assam not far behind. This does not appear to be associated with epidemic conditions except in Bengal. Lieut.-Colonel Sokhey discusses the present position of plague in India. It is still a serious problem although we have now a comprehensive idea of the disease, calcium cyanide compounds of rats and fleas, a potent prophylactic vaccine and sulphonamides in treatment. It is suggested that a central organization should be formed to direct and control anti-plague measures all over India. There is a note on the malaria situation in Bengal in 1943 by Brigadier Covell. In this year epidemic conditions prevailed over most of the province, and there was a high mortality rate in certain areas, the factors which contributed to the severity of the epidemic being famine conditions and the influx of Burma evacuees and of non-immune military personnel. The only anti-malaria measures applicable in rural areas of Bengal at present is the provision of adequate drug treatment for the sick, but at the early stages of the epidemic grave difficulties were experienced in securing effective distribution of quinine. The volume also contains abstracts from foreign papers and public health notes and news.

We welcome the gazette and wish it all success. It will henceforth appear from time to time as fresh material becomes available.

THE SCOPE AND FUTURE OF PHARMACOLOGY IN INDIA

SPEAKING on the above subject as President of the Physiology Section of the 32nd Indian Science Congress (1945) Dr. B. Mukerji said that pharmacology is a much neglected branch of science in India. The standard of teaching is poor, and the quantity and quality of research output are also poor. The collaboration that should exist between chemists, bacteriologists and pharmacologists has not been developed, though happily here a reorientation in outlook is growing. It is a good sign that manufacturing firms are taking interest and voluntarily planning to organize their pharmacological laboratories. Dr. Mukerji suggests the establishment of a National Institute for Drug Research so that all work can be done in close co-operation with a group of specialists housed in the same institution. Continuing, he said that the quality of drugs offered for sale in India is far from ideal, especially in the matter of proprietary medicines which are usually sold with the most exaggerated and fantastic therapeutic claims, and the composition of which is generally kept secret. An extensive survey, a few years ago, showed that as many as 49 per cent of the drugs in the market were not genuine and below par in quality or potency. Some legislative action has since been taken, but a more energetic action is needed. Dr. Mukerji recommends the formation of an Indian organization on the lines of the Council of Pharmacy and Chemistry of the American Medical Association in order to bring before the profession the truth concerning proprietary medicines, and in order to assist in the clinical trial of drugs there should also be a therapeutic trials committee.

Public Health Section

THE PARASITOLOGY OF MALARIA AMONG DESTITUATES IN CALCUTTA DURING AND AFTER THE BENGAL FAMINE OF 1943

By B. M. DAS GUPTA

and

L. B. SIDDONS

(From the Department of Protozoology, School of Tropical Medicine, Calcutta)

DURING the summer of 1943, Bengal was in the grip of one of the worst famines on record for the province, and large numbers of destitute persons flocked to Calcutta, mainly from the neighbouring districts, viz, 24-Parganas, Hooghly and Midnapur. This influx of destitutes continued for several months. As these people suffered from fever and showed a high mortality, an investigation was started on the 25th September, 1943, for examination of blood smears of destitute children at the Lee Memorial Relief Hospital. Next month, one of us (L. B. S.) also began collecting blood smears from destitute persons on the streets of Calcutta in connection with a study of malaria transmission by *Anopheles stephensi*. As the street collection was not satisfactory, the Campbell Hospital which was then the main centre for

Tropical Medicine. Material for this work was obtained from the Behala Relief Hospital which was an important receiving centre for sick destitutes, the large destitute camp established at Narkeldanga under the auspices of the Bengal Relief Committee, the Marwari Relief Hospital and a few other relief hospitals which were opened to meet the emergency.

Methods

In view of the high mortality among the destitutes, which was in many cases due to malaria, immediate reports had to be sent to the hospitals on the blood findings. As ordinary methods of staining blood smears took considerable time, we resorted to Field's technique of staining thick smears (Field, 1941). We are indebted to Dr. J. Lowe, Professor of Tropical Medicine, for his suggestions in this matter. By this method smears take but a few seconds to stain. Thin films were also examined when specific identification was in doubt, especially in scanty infections and in cases of suspected mixed infections involving 'ring' forms. About 3 minutes were spent in examination of thick smears. The bulk of the material was examined by Mr. R. K. Maitra, technical assistant in the department, under the supervision of the authors. Except possibly in the case of smears from the Lee Memorial Hospital which were not prepared by our assistants, there was no selection of fever cases.

Incidence of malaria

Between 25th September, 1943 and 31st December, 1944, 14,862 destitutes were examined; 4,920 were positive for malaria parasites, an incidence of 33.1 per cent.

The monthly variation in the incidence of infection is shown in table I and figure 1. The incidence of 44.0 per cent in December 1943 was probably maximal for that year. Thereafter the curve falls steadily to a minimum of 14.7 per cent in June

1944 and then commences to rise sharply in July, reaching its peak of 51.7 per cent in November 1944, after which it appears to decline. In broad seasonal trends this curve approximates to the normal curve of incidence for the plains of Bengal as worked out by Knowles and Senior White (1930) and Knowles and Basu (1934), though their data relate to monthly incidence among total

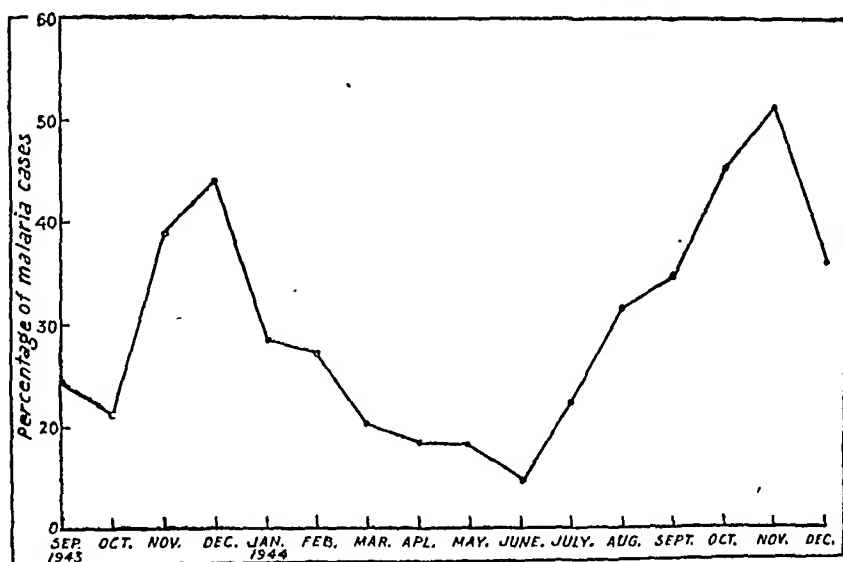


Fig. 1.—Incidence of malaria among destitutes in Calcutta.

the treatment of sick destitutes was tried, and Dr. Aich, the then physician-in-charge of the destitutes at this hospital gave us every facility in this work, and we are greatly indebted to him in this matter. In November 1943, in connection with an official investigation on the health problems of starvation under the auspices of the I. R. F. A., the examination of blood smears was carried out by the School of

malaria. Knowles and Senior White's chart drawn on the same scale as figure 1 is given in figure 2. A striking feature of the famine malaria curve is that the peak in 1943 occurred in December, when, under normal conditions, malaria incidence shows a definite decline.

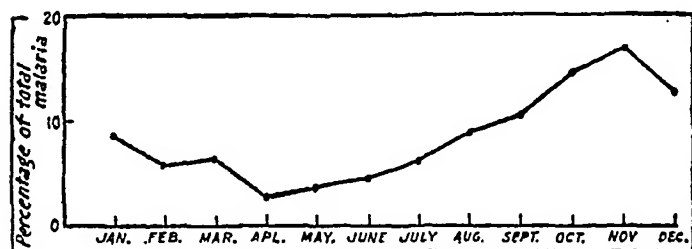


Fig. 2.—Incidence of malaria in Calcutta over the year. (Knowles and Senior White, 1930.)

Correspondingly in 1944 the minimum incidence was recorded in June when it normally occurs in April. There is no evidence of any spring malaria in that year. These features will be commented on again when the prevalence of the different species of malaria is considered. The incidence was actually higher in 1944 than in 1943. This was probably not due to infection contracted locally during the epidemic of 1944 in the eastern suburbs of Calcutta where the destitutes were encamped, since the films were taken from the destitutes soon after their arrival at the camp.

Incidence of malaria by species

Considering the findings of the entire period of observation, *P. falciparum* and *P. vivax* formed 48.8 and 49.7 per cent respectively of the total positive findings, while *P. malariae* was conspicuously rare with a proportion of only 1.4 per cent. The proportion of *P. falciparum* is very nearly normal. The normal proportion of *P. malariae* in Bengal according to Knowles and Senior White (*loc. cit.*) is about 12 per cent; in Hooghly district, Iyengar (1932) found it to be 14.4 per cent. Therefore, during 1943 and 1944 *P. vivax* had apparently increased at the expense of *P. malariae*.

The seasonal distribution of the species estimated on total monthly malaria in each month is indicated in table I and plotted in figure 3. The corresponding chart for

Calcutta from Knowles and Senior White's memoir is given in figure 4 for comparative study. The curves for *P. falciparum* and *P. vivax* obtained by Iyengar (*loc. cit.*) are essentially similar to those plotted by Knowles and Senior White.

As under normal conditions, *P. falciparum* was the dominant species during the epidemic waves of 1943 and 1944. This is suggested by the close agreement between the curves for this species and for malaria incidence. But there is no minor spring rise as found by Knowles and Senior White (figure 4) in March and by Iyengar (*loc. cit.*) in May. The curve of *P. vivax* is decidedly unusual. It had already commenced to rise during the autumnal epidemic of 1943, whereas normally it is at its lowest then, and its rise usually comes in February. From November 1943, the curve for *P. vivax* rises fairly steadily to a peak in August, which is about four or five months later than its normal peak, as reference to figure 4 indicates. During the epidemic of 1944 there was, therefore, a higher proportion of *vivax* malaria than usual. This accords with the definite impression that the epidemic of 1943 was severer both in the intensity of infections seen, particularly those due to *P. falciparum*, and in respect of mortality among the destitutes, though earlier diagnosis and

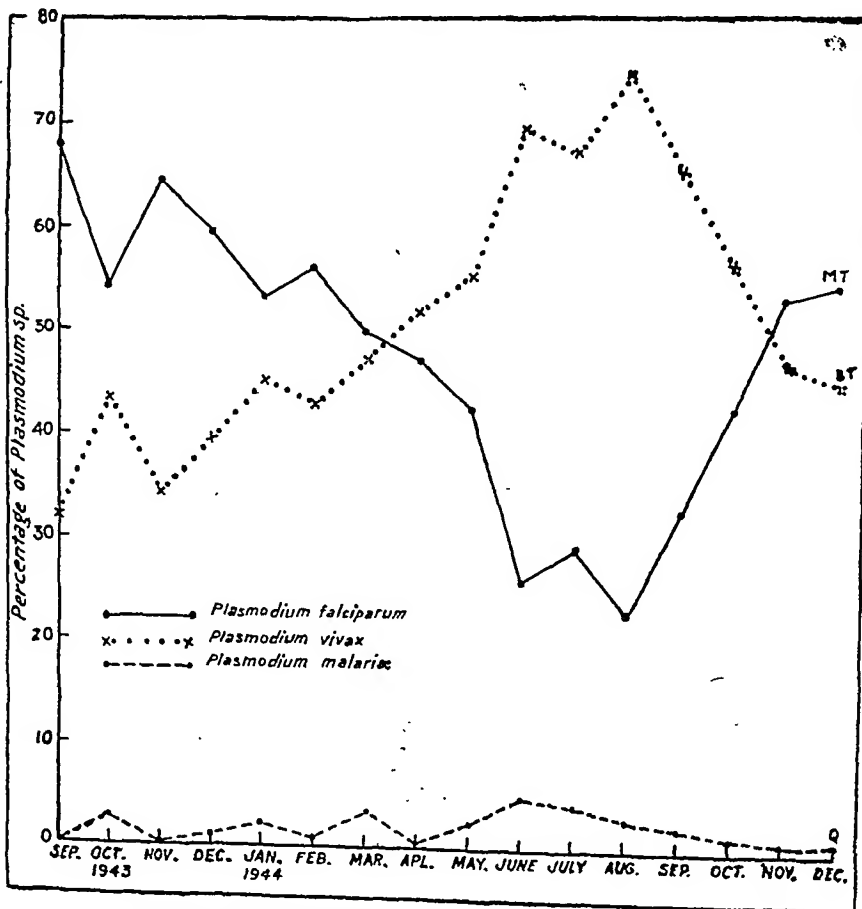


Fig. 3.—Seasonal distribution of malaria species among destitutes in Calcutta.

TABLE
Malaria incidence

		Sept. 1943		Oct. 1943		Nov. 1943		Dec. 1943		Jan. 1944		Feb. 1944		March 1944	
		Number examined	Number positive	Number examined	Number positive	Number examined	Number positive	Number examined	Number positive	Number examined	Number positive	Number examined	Number positive	Number examined	Number positive
Street collection	199	38
Lee Memorial Relief Hospital (Elliot Road Orphanage).		91	22	52	10	82	21	41	18	53	10	36	10	45	8
Marwari Relief Hospital		45	20	7	3	173	27	145	28
Narkeldanga Relief Camp.		292	121	517	231	704	214	1,401	402	542	112
Suresh Sarkar Road Hospital.		101	35	77	14
Campbell Hospital	673	149
Lake Club Hospital	146	54	58	25
Behala Hospital	502	204	188	89	2	1
Total ..		91	22	924	197	1,022	400	950	418	843	242	1,610	439	732	148
PERCENTAGE ..		24.1		21.3		39.1		44.0		28.7		27.2		20.2	
Species distribution of total malaria (percentage).	M.T.	68.1		54.2		64.7		59.8		53.0		56.3		49.6	
	B.T.	31.8		43.2		34.7		39.2		45.0		42.8		47.0	
	Q.		2.6		0.6		0.9		2.0		0.9		3.3	

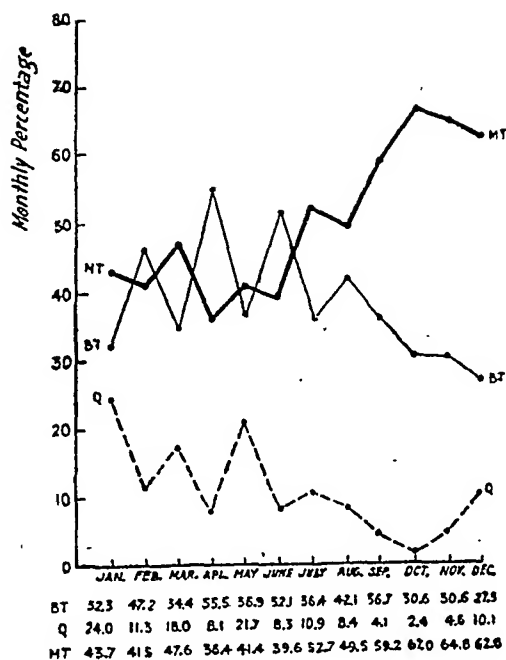


Fig. 4.—Seasonal incidence of malaria species in Calcutta for one year. Combined figures from Megaw, Rogers, and Knowles and Das Gupta—1,238 cases in all.

treatment and the somewhat better condition of the people in 1944 also had much to do with these facts. Thus during the famine and post-famine periods there seems to have been more *vivax* malaria than usual, possibly due to more relapses caused by undernutrition and inadequate treatment due to acute shortage of anti-malarial drugs. *P. malariae* was too rare throughout the investigation to merit any discussion.

Mixed infections

Among 4,474 positive smears examined between 25th September, 1943 and 30th November, 1944, 152 cases of mixed infection were recorded, a rate of 3.4 per cent. The monthly incidence is indicated in table II. Mixed infections seem to have been commoner during January to March and September to November in 1944 than in other periods covered by the investigation. The distribution of the types of mixed infection was as follows:—

	Per cent
<i>P. falciparum</i> and <i>P. vivax</i> ..	91.4
<i>P. falciparum</i> and <i>P. malariae</i> ..	4.6
<i>P. vivax</i> and <i>P. malariae</i> ..	2.0
All three species ..	2.0

The total incidence is similar to that recorded by Knowles and Senior White (*loc. cit.*) who

I

among destitutes

April 1944		May 1944		June 1944		July 1944		Aug. 1944		Sept. 1944		Oct. 1944		Nov. 1944		Dec. 1944	
Number examined	Number positive	Number examined	Number positive	Number examined	Number positive	Number examined	Number positive	Number examined	Number positive	Number examined	Number positive	Number examined	Number positive	Number examined	Number positive	Number examined	Number positive
..
30	11	20	6	22	3	53	13	31	10	6	4	18	9	3	3	13	6
143	26	176	33	59	7	104	20	152	26	112	25	157	49	238	93	210	81
482	85	599	100	339	52	384	96	845	292	990	355	1,192	590	1,295	698	1,017	359
..
..
..
655	122	795	139	420	62	541	129	1,028	328	1,108	384	1,367	648	1,536	794	1,240	446
18.6		16.5		14.7		22.4		31.9		34.7		47.4		51.7		35.9	
47.2		42.5		25.8		28.7		22.7		32.5		42.3		52.6		54.1	
52.0		55.3		69.4		67.2		74.6		65.2		56.5		46.5		44.9	
0.6		2.1		4.8		4.1		2.7		2.2		1.2		0.8		0.9	

considered such a figure too low. It was our experience that during January to March of 1944, 59 per cent of 27 destitutes admitted to the Carmichael Hospital for Tropical Diseases

and followed up with daily blood examinations for several days, proved to have mixed infection with *P. falciparum* and *P. vivax*. Therefore the true incidence was undoubtedly higher

TABLE II
Mixed infections

	<i>P. falciparum</i> and <i>P. vivax</i>	<i>P. falciparum</i> and <i>P. malariae</i>	<i>P. vivax</i> and <i>P. malariae</i>	Three species	Total	Percentage of total monthly malaria
September 1943 ..	1	..	1	..	2	9.1
October 1943 ..	4	4	2.0
November 1943 ..	13	13	3.2
December 1943 ..	9	1	..	1	11	2.6
January 1944 ..	11	1	12	4.9
February 1944 ..	15	1	16	3.6
March 1944 ..	6	6	4.0
April 1944 ..	3	3	2.4
May 1944 ..	1	1	2	1.4
June 1944
July 1944	1	..	1	0.8
August 1944 ..	9	9	2.7
September 1944 ..	15	1	16	4.2
October 1944 ..	21	3	24	3.7
November 1944 ..	31	..	1	1	33	4.1
TOTAL ..	139	7	3	3	152	3.4

than was revealed by the methods followed in this investigation.

Summary and conclusions

The incidence of microscopically diagnosed malaria among 14,826 destitutes examined during and after the Bengal famine of 1943—from 25th September, 1943 to 31st December, 1944—was 33.1 per cent. Peaks in the curve of monthly incidence occurred in December, probably, in 1943 with a rate of 44.0 per cent and in November in 1944 with a rate of 51.7 per cent. Both the peak incidence in 1943 and the minimum monthly incidence in 1944 occurred later than usual. *P. falciparum* and *P. vivax* contributed about equally to form 99.0 per cent of the total malaria, and *P. malariae* was only 1 per cent. The proportion of *P. falciparum* infections was normal and this species showed its

usual predominance during the autumnal epidemics. The proportion of *P. vivax* infections appeared higher than usual both among total malaria and during certain seasons. There was no normal spring rise in 1944, but a steady increase of *P. vivax* infections from November 1943 to a very late peak for this species in August 1944. The proportion of mixed infections was much higher in destitutes followed up in hospital for several days than among those examined on a single occasion.

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Current Topics

The Peckham Experiment

(From the *Medical Press and Circular*, Vol. CCXI, 19th April, 1944, p. 241)

THERE are fashions in everything, as we have more than once remarked before now, including medical thought and its expression. A few years ago there was a phrase on every lip that came precious near degenerating into the cant of which Dr. Johnson was so anxious we should clear our minds—that phrase was 'Positive Health'. Nor was its popularity decreased by the fact that most people were not at all sure what they meant by it; rather perhaps was it enhanced. To-day it has been replaced by another phrase—'Health Centre'. While this is far less vague it is, in fact, something of a misnomer. A Health Centre should surely be a place where health is studied, preserved, and if possible improved, rather than a group clinic for the treatment of disease. Yet this last function will constitute the main activity of the Centres as proposed in the National Health Service.

This distinction, subtle perhaps, but quite valid and definite, is underlined by the latest report from the first, the Pioneer Health Centre which founded in 1926, has now evolved into the 'Peckham Experiment'. Here the aim was not at all to treat disease, but to preserve health and avert disease by periodical medical examination. This led in turn to a study of the many facets and degrees of health itself (one result of which was to show that some 60 per cent of 'healthy people' suffer from one disorder or another which, however, they are able to compensate) and to a natural extension of the enquiry into the origins and conditions of health. It was soon realized that for this purpose the family rather than the individual must be regarded as the unit for study, since such a study to be complete must begin with the individual *in utero* and follow him through infancy, childhood and adolescence to the adult state.

Accordingly the new Centre, built in 1935, was designed primarily, one might say, as a family club with medical facilities available. These medical facilities were in their way very complete. Periodical overhauls, ante-natal and post-natal care and advice, pre-marital consultations, parental consultations, infant care and vocational guidance were all to be had, a great feature being the preliminary talk on joining and

the consultation which took place as soon as pregnancy had begun. This last was strongly encouraged and seems to have been of particular value, as was the ante-natal care. Delivery was conducted in hospital by arrangement, but the new mother merely stayed in overnight and came home next day to be looked after and set on the right lines by the Centre's nursing staff.

From the purely medical point of view the results achieved were interesting, but by no means startling, and merely went to confirm the findings of the previous investigations which have already been published. Where the experiment broke new ground was in the field of what we might now call social biology. And although in this respect it could hardly be as complete as a survey which would embrace working and home conditions in addition to the recreational aspect, nobody can doubt that the staff of the Centre obtained a most valuable insight into the operation of human biology in a modern urban industrial community, and unique experience in the treatment of the biological, as distinct from the pathological, lesions that result from such an artificial and spiritually sterilizing existence. It is the authors' thesis—not to be disputed—that each of us must live in symbiosis with our environment. If this symbiosis is incomplete, not to say absent, if we are at logger-heads with our environment, health is impossible. Much of present-day social pathology derives from the fact that, so far from forming a community, we exist in isolated autonomous units geographically integrated, but socially and spiritually discrete. The results are ignorance, failure to develop, lack of interest in life, and not infrequently, vice or disease.

About six hundred families were members of the Centre when the outbreak of war forced it to close. For the sum of a shilling a week or thereabouts they had access to a swimming pool, games of all kinds and provision for meals (which, however, they had to prepare and serve themselves). There were dances, concerts and theatrical entertainments, and by and by they acquired a country camp. For certain games an extra fee had to be paid, but it was not much. All social classes were represented, since the district served was by no means impoverished, but the average family income averaged from £3 to £3 10s. per week. What we might call the material, therefore, provided a thoroughly representative section of the population as a whole.



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And the results of the experiment? One result, which we do not hesitate to describe as of national importance, was the distinct alteration in the attitude towards children. Young couples, previously childless, frequently decided to have a family. Others decided to add to theirs. All became far more sensible and efficient parents. Mothers of families had a place where they could leave their children with confidence while they themselves could take a few hours off in recreation. Biologically and socially the educational value of the Centre was enormous. Incompetent mothers could learn to cook, to knit, to sew, no less than to dance or swim; they could get advice on their problems, they got to know their neighbours and to make friends. In short, they began to make contact with their environment at dozens of new points and to share the experience of helping and being helped. Thus, the isolated units became a community, immensely stronger and healthier as a result.

We would advise our readers to make it their business to study this book. It foreshadows, in our view, a development that must occur in our profession sooner or later. Financially and economically it is quite feasible. And it may well represent the point at which 'Positive Health' and 'Health Centres' cease to be nebulous concepts or misnomers and emerge into reality.

Vaccines for Epidemic Encephalitis

(From the *Medical Press and Circular*, Vol. CCXI, 19th April, 1944, p. 243)

THE St. Louis and Japanese B types of epidemic encephalitis occur in the late summer and early autumn, and are caused by two immunologically distinct viruses. The most recent evidence favours the idea that these viruses exist in an animal reservoir and are transmitted by mosquitoes. The St. Louis virus has so far only been isolated in America, but the Japanese B type is more widespread.

Many attempts have been made to prepare non-infective vaccines, and Sabin, with his collaborators now present preliminary data about one which promises to be successful. Strains of virus were selected which yielded high titres in the brains of two to three weeks old mice. Virus grown on eggs and in the brains of hamsters and young sheep was found to be unsatisfactory for various reasons. The vaccines consist of uncentrifuged 10 per cent mouse brain suspensions in isotonic saline solution in which the virus has been rendered non-infective by 0.2 per cent formaldehyde, the inactivation having taken place at a temperature of two to three degrees C. The vaccines retained their potency only when stored in the cold, and when various measures had been taken to neutralize the formaldehyde. The vaccines were effective in producing resistance against infection by peripheral routes such as the intravenous or intraperitoneal, and it was only when large and multiple doses were given to mice that it was possible to induce resistance to 10-100 M.L.D. of virus given by the intra-nasal or intracerebral routes. Tests on human volunteers indicated that two doses of 2 c.c., given three days apart, could be administered without fear of local or systemic reactions. This dose of vaccine contained enough antigen to stimulate the development of neutralizing antibodies in about 50 per cent of adults. It is obvious that no tests on a wide scale can be done until an epidemic occurs, but the preliminary data presented are full of promise.

The Sterno-mastoid Sign

By A. W. BRANWOOD, M.B., Ch.B.

(Abstracted from the *Edinburgh Medical Journal*, Vol. LI, March 1944, p. 152)

THE sterno-mastoid sign was first described by Trail in a paper on the 'Early Diagnosis of Tuberculosis'. He pointed out that a patient with a unilateral and

early lesion in the chest will show this sign on the same side as the lesion, thus warning the physician of an abnormality which requires investigation. A positive sterno-mastoid sign indicates displacement of the mediastinum to that side, and it may even be present before there is any x-ray evidence of mediastinal shift.

To elicit the sign the head is supported on a pillow or by the examiner's hand and the patient is told to look straight in front of him. The sign is regarded as positive when the tendinous portion of the sterno-mastoid muscle on one or other side is more tense than its fellow. Even when the position of the head is changed by slightly turning to one or other side the increase in tension in the affected muscle can still be appreciated. In cases where there is a gross lesion the sign can be noted by simple inspection; the muscle on the affected side is very prominent and is obviously very tense. Even in early cases the sign can always be elicited by palpation. The tendinous portions of the sterno-mastoid muscles are gently palpated at their attachment to the manubrium sterni. Any increase in tension of one or other muscle is very easily felt and indicates a positive sterno-mastoid sign on that side. It is a much easier sign to elicit and less disturbing to the patient than examination for displacement of the trachea, which entails deep palpation in the supra-sternal notch.

Plague: Sulphadiazine Treatment of Guinea-pigs Infected by Artificial Methods or by Flea Transmission

By N. E. WAYSON

and

M. C. McMAHON

(Abstracted from the *Public Health Reports*, Vol. LIX, 24th March, 1944, p. 385)

FIFTEEN guinea-pigs were inoculated intradermally with virulent *P. pestis* and developed plague, but 13 recovered after treatment with sulfadiazine and showed no evidence of infection at necropsy when killed 21 days after inoculation, and one died with sulfonamide crystals in the kidneys. Thirteen untreated controls died of plague after similar inoculation. One control died of hæmorrhage 3 days after inoculation without evidence of plague; one control was killed the thirty-fourth day after inoculation and plague was proved bacteriologically at necropsy.

Eleven guinea-pigs infected with plague by flea bites developed the disease, but 7 recovered under treatment with sulfadiazine and showed no evidence of the infection at necropsy 21 days after inoculation. Nine untreated controls which were infected in a similar manner developed the disease and died.

These experiments indicate that the administration of sulfadiazine to guinea-pigs in which buboes of plague have been contracted by flea transmission or have been induced by artificial methods simulating flea transmission is of very definite remedial value. The drug treatment should begin as soon as the characteristic buboes and fever have developed and should continue through the febrile period. A blood level of 4 to 7 mg. per cent of the drug was usually maintained, but no attempt was made to determine the level required for therapeutic efficiency.

The similarity of the evolution and manifestations of plague induced in guinea-pigs and in man by flea transmission lead to the conclusion that this drug may be of great value in the therapy of bubonic plague in man previous to the development of a generalized bacteraemia.

Glucose: Its Uses and Abuses

(From the *East African Medical Journal*, Vol. XXI, May 1944, p. 129)

THE study of the metabolism of digestion has brought to light a number of facts about the absorption

and excretion of the various sugars in food that are not always generally appreciated. For example, the amount of any sugar absorbed from the stomach is negligible, unless it is present in very concentrated form—say a 40 per cent solution—such as never occurs in normal circumstances. Similarly, there is no variety of sugar that is absorbed from the large intestine and rectum; hence all sugars are valueless in nutrient enemata where they are so often to be found. The fact is that the absorption of sugars takes place in the small intestine only, normally; and only the monosaccharides or hexoses—glucose, fructose, galactose, mannose—and the pentoses, xylose and arabinose, can be absorbed directly. The disaccharides, cane sugar, beet sugar, maltose, and lactose or milk sugar, must first be hydrolysed, each into its two component hexose molecules, before they can be absorbed by the intestinal mucosa and passed on into the blood stream. This hydrolysis is brought about fairly rapidly in the stomach by the hydrochloric acid of the gastric juice and does not there call for any process of digestion by ferments. Further, the hexoses and pentoses from the carbohydrate foods are absorbed from the small intestine at different rates, which have been figured as follows: d-galactose 110; d-glucose 100; d-fructose 43; d-mannose, a stereoisomer of d-glucose, at no more than 19; l-xylose 15; l-arabinose 9. It is remarkable that the rate of absorption of these sugars is independent of the concentration of the solution administered, of the size of the dose, and of the concentration of the glucose in the blood. In other words, the intestinal mucosa guards the organism against sudden and large influxes of sugar, and must be regarded as an important factor in the regulation of carbohydrate metabolism. Given intravenously or by hypodermic injection the hexoses are absorbed and utilized, while the disaccharides are excreted complete and unchanged in the urine. And it is worth noticing that many of these sugars have been given a number of names which naturally leads to confusion in the lay mind. Thus cane sugar is also known as d-sucrose, saccharose, saccharobiose; maltose as malt sugar maltobiose; lactose as milk sugar, lactobiose; glucose, the worst offender, as d-glucose, d-dextrose, dextrose, grape sugar: fructose as d-fructose, laevulose, fruit sugar.

The conclusion is that glucose enjoys a clinical vogue or reputation that it does not in the least deserve. Nowadays it is administered broadcast to the sufferers in our nursing homes and hospitals, so far as the lessened supplies available in war-time allow, the mawkishness of its flavour sometimes enhanced rather than mitigated by the addition of sodium bicarbonate, itself another of our doctors' favourites. Patients are encouraged to think that they are not being properly treated if they do not get their dollop of glucose day by day. Athletes, a notoriously simple race of men, read and presumably believe that glucose improves athletic performance out of all knowledge. Mothers are informed, perhaps merely for the sake of the alliteration, that glucose builds bonny babies; and indeed, if the babies get a glucose enriched by the addition of vitamins A or A and D as in some of its proprietary forms, then the mixture will surely help the building. Yet, however, true or fanciful these various claims may be, in view of the facts about the fate and absorption of the various sugars quoted above, there is nothing to show that say half an ounce of glucose taken by the mouth gets into the blood stream any quicker than half an ounce of cane or milk sugar similarly consumed. This view is, indeed, confirmed by the experience of the many diabetic patients who carry either cane sugar, glucose, or ordinary sweets about with them always, for the prompt treatment of the insulin reactions or the sudden onset of hypoglycaemia to which they are liable, and find the one as good as the other for this purpose. At the present time glucose costs ten or fifteen times as much as cane sugar, and is hard or impossible to come by. There are, of course, among us those who hold that as glucose is more expensive it must be 'better' for them than the more vulgar cane sugar. But this form

of carbohydrate snobbishness will not appeal to many. A return to cane sugar in the form of the *Eau Sucree*, told of in one of Thackeray's 'Roundabout Papers' and a well-ried domestic remedy in days of sickness for the last two centuries and more, seems to be indicated. And glucose should in general be reserved mainly for emergency administration by intravenous injection, and be given by the mouth only to such patients as prefer its flavour and action to those of other cheaper varieties of sugar.

Myasthenia Gravis : A Consideration of Its Causation in a Study of Fourteen Cases

By A. WILSON

and

H. B. STONER

(Abstracted from the *Quarterly Journal of Medicine*, Vol. XIII, January 1944, p. 1)

THE following conclusions are based on a study of 14 cases of myasthenia gravis; the report includes a record of the occurrence of the disease in a newly born infant.

1. The serum cholinesterase activity of patients with myasthenia gravis is not greater than that of normal adults. There is no evidence that the muscular weakness in myasthenia gravis is due to an excessively rapid destruction of acetylcholine by cholinesterase.

2. Patients with myasthenia gravis are able to synthesize acetylcholine in sufficient amounts to produce the normal 'muscarine' effects on glands and involuntary muscle. These effects have been increased by the administration of pilocarpine.

3. Exposure to sunlight causes an increase in the severity of the symptoms and signs.

4. By means of cine-camera and ergograph studies it has been shown that exercise of a remote group of muscles produces an increase in the severity of the signs.

5. The serum of patients with myasthenia gravis not under prostigmin treatment, when tested on the isolated nerve-muscle preparation of the frog, produces a block in neuromuscular transmission. This effect is not obtained with serum collected from patients during prostigmin treatment.

6. The blood of patients with myasthenia gravis contains a substance, partially soluble in alcohol, which interferes with neuromuscular transmission. The rôle of this substance in the causation of myasthenia gravis is discussed.

The Indian Journal of Medical Research

Vol. XXXII, No. 1, May 1944

THE following is the list of contents:—

- (1) Tang, F. F., Chu, C. M., and Wong, Y. W. A study of *Vibrio cholerae* isolated from the 1942 Kunming epidemic, with special reference to serological types.
- (2) Bose, B. C., and Ahuja, M. I. Detection of pyrogens in fluids by biological methods (with 2 graphs in text).
- (3) Banerjee, R. Some observations on Voges-Proskauer test.
- (4) Sen, S. N., and Basu, P. N. Enhancement of diphtheria toxin production by glycolysis.
- (5) Greval, S. D. S., and Bhattacharji, J. N. Some physical and immunological differences between natural and re-constituted human serum.
- (6) Mason, Eleanor D. Daily measurements of basal metabolism, body temperature and pulse rate during a journey to the tropics (with 1 graph in text).
- (7) Patwardhan, V. N., Chitre, R. G., and Sukhatankar, D. R. Studies in calcium and phosphorus metabolism. Part VI. The ionic products of calcium phosphates in blood serum of rachitic infants (with 1 graph in text).

- (8) Swaminathan, M. Nicotinic acid content of Indian foodstuffs.
- (9) Day, C. D. Marshall, and Shourie, K. L. The incidence of periodontal disease in the Punjab.
- (10) Gupta, J. C., and Kahali, B. S. General pharmacology of *Umbellatine*, a new alkaloid isolated from *Berberis umbellata* Wall. and *Berberis insignis* Hook. f. and its use in the treatment of oriental sore.
- (11) Ray, N., and Basu, U. P. Influence of phenols on phenol reagent.
- (12) Bose, A. N., and Ghosh, J. K. Studies on sulphanilyl-benzamide: toxicity and absorption.
- (13) Bose, B. C., and Mukerji, B. Use of trichlorethylene as an anaesthetic agent: an experimental study on laboratory animals (with 1 plate).
- (14) Cooray, G. H. Observations on malignant disease in Ceylon based on a study of 2,295 biopsies of malignant tumours (with 2 graphs in text).
- (15) Reddy, D. Govinda, and Rao, S. V. Raja. Blood and bone-marrow in pre-cirrhotic toxic splenomegaly due to manganese (with 1 plate).
- (16) Majumder, D. N., and Das Gupta, C. R. Haematological studies in *Silenus (Macacus) rhesus*. Part I. The blood picture of the normal monkey (with 8 graphs in text).
- (17) Siddiqui, M. A. H., and Shah, M. A. Estimation of stature from long bones of Punjabis.

The following are the authors' summaries and conclusions:—

(1) A study of the strains of cholera vibrio isolated from the 1942 Kunming epidemic with special reference to the existence of serological sub-types was conducted. Altogether 129 specimens from 110 cases of typical clinical cases of cholera have been studied and from them 83 strains of vibrio have been isolated including two inagglutinable strains. Most of the strains have been tested against stock cholera serum, Inaba and Ogawa specific sub-type sera and it was found that out of 69 strains thus tested, 64 strains belonged to the Inaba sub-type (93 per cent) and 15 strains belonged to the Ogawa sub-type (7 per cent). The origin of the Ogawa sub-type has been discussed and the significance of the two serological types given. No 'intermediate' type was recovered from the epidemic, but in going over some of the old stock cultures, two suggestive strains have been found.

(2) A detailed investigation on the suitability of biological tests for the detection of pyrogens in fluids used for intravenous injection has been carried out. Normal temperature variations in 100 rabbits has been worked out. The precautions, necessary for carrying out the hyperpyrexia test with accuracy, following injections of pyrogenic fluids in rabbits, have also been described.

Two strains of pyrogenic organisms have been isolated from a sample of water from a public reservoir and their characters studied.

A comparison of the hyperpyrexia and leucopenia tests as carried out in rabbits using suspensions of these two organisms showed that while the former is a fairly satisfactory method of pyrogen estimation, the latter has not been found suitable for this purpose.

(3) Even under optimum conditions the original Voges-Proskauer test is never so satisfactory as the Barrett test and the latter is best done after two days' or even one day's incubation at 37°C. in glucose-phosphate or glucose-peptone medium. If it is desired to do the V.P. or Barrett test after the usual three days' incubation, instead of after one day's incubation, glucose-peptone of pH 8 should be used in place of glucose-phosphate medium.

(4) From the results given in the text it appears that there is significant enhancement of diphtheria toxin production, using a veal infusion prepared in the manner described which favours the glycolytic production of sarcolactic acid. This medium is inexpensive and can be easily prepared in any bacteriological laboratory. Observation over a prolonged period has shown that there is no marked seasonal variation in the results.

(6) On a journey from San Francisco to India a woman whose basal metabolism was known to be 10 per cent lower in the tropics (Madras) than in a temperate climate (New York and Boston) was measured daily with the purpose of finding out how long an exposure to the tropics was necessary for this adaptation in heat production to be established. The measurements were made before rising in the morning, with a Benedict-Roth metabolism apparatus. The conditions throughout the journey were approximately uniform with respect to diet and activity and the transition from comfortably cool to hot humid tropical climate was abrupt.

On the first two days after exposure to tropical heat both the basal metabolism and oral temperature rose slightly. From the third day the metabolism began to fall and at the end of a week in the tropics was 10 per cent lower than the average rate for this subject in temperate climate. During the second week it fluctuated and fell slightly more. The oral temperature did not return to this subject's normal until the end of the second-week and it is suggested that the second week was a period of stabilization of the heat balance.

These results are consistent with those of a similar experiment on himself reported by Martin, and support the hypothesis that the mechanism for this relatively slow adjustment of heat production on entering the tropics, beginning about the third day and not completed for approximately one week, is reduced activity of the thyroid gland.

A brief comparison is made of these tropical studies with laboratory studies by other workers on the effect of artificially regulated temperature changes.

(7) The blood serum of 79 cases of suspected or frank rickets in infants and children were analysed for calcium, inorganic phosphorus and total protein. Samples of blood serum from 11 normal children were also similarly analysed.

The concentration of Ca^{++} , $\text{HPO}_4 =$ and $\text{PO}_4 \equiv$, at pH 7.4 and the solubility products of $[\text{Ca}^{++}] \times [\text{HPO}_4 =]$ and $[\text{Ca}^{++}] \times [\text{PO}_4 \equiv]^2$ were calculated from the data.

It was found that the pK s.p. values of CaHPO_4 in rachitic cases were over 5.7 in 77 out of 79 cases, whereas in only one out of 11 non-rachitic children was the value above 5.7. With regard to the pK s.p. of $\text{Ca}_3(\text{PO}_4)_2$, 77 out of 79 cases had values above 23.0 showing undersaturation whereas in two cases out of the 11 non-rachitic children the blood was undersaturated with respect to this latter salt.

(8) The nicotinic acid content of about 160 food-stuffs has been determined by an improved chemical method using the cyanogen bromide and aniline reagent.

Of the foods tested, dried brewer's yeast, liver, rice polishings (from raw paddy) and pea-nuts are rich sources.

Meats of various kinds are good sources and fish a fair source of nicotinic acid.

Among the cereals, whole wheat, unmilled rice, whole barley, parboiled rice and pearl millet are good sources, containing 2 to 3 times as much nicotinic acid as white flour, maize, oatmeal, certain millets and raw milled rice. Maize, which is known to be associated with pellagra, gave a low value; but similar low values were also obtained for white flour, oats, milled raw rice and certain millets. Italian millet contained only half as much nicotinic acid as that found in whole maize.

Cow's milk, eggs, fresh vegetables and fruits are in general poor sources of nicotinic acid.

(9) The incidence of gingivitis and pyorrhoea in hospital patients, police constables and school children in Lahore has been investigated. Both conditions were found to be very common. The frequency of gingivitis decreased with age and that of pyorrhoea increased, so that the latter appears to be a later stage of the former.

Except in the age group 21-30, the incidence was similar in both sexes. In the age-group in question, females showed less periodontal disease.

The incidence of periodontal disease was similar in vegetarians and non-vegetarians.

(10) *Umbellatine*, like berberine, is not a proto-plasmic poison.

It has a specific inhibitory action on the growth of *Leishmania tropica*—the causative organism of oriental sore.

It has a depressant action on the cardiovascular system. The heart is depressed directly. Blood vessels are dilated directly and also perhaps by stimulation of the parasympathetic vasodilator nerve-endings.

The smooth muscles of spleen, intestine, uterus and bladder are stimulated. In some of these the action seems to be due to the stimulation of the parasympathetic nerve-endings of the muscles concerned.

Respiration is depressed and bronchi constricted.

Umbellatine has been used with success in the treatment of oriental sore.

The pharmacological actions of *Umbellatine* are similar to those of berberine but more intense except in producing cardiovascular responses which are less than those caused by berberine.

Salts of *Umbellatine* are less soluble than the base itself. With urea a more soluble product has been obtained.

(11) The behaviour of phenols with phenol reagent is dependent on the nature and position of the substituent in the phenol molecule. Nitro group, when present in the para position, does not reduce phenol reagent, whereas the hydroxy group in the same position enhances the reducing capacity to a very considerable extent.

p-chloro-m-cresol, p-cresol, m-cresol, and p-chloro-phenol can easily be estimated in solution with a phenol reagent.

(12) The results obtained indicate that sulphanilyl-benzamide is free from undue toxicity, and that it appears to be better tolerated than sulphanilyl-guanidine (cf. Marshall *et al.*, 1940). Absorption from the gastrointestinal tract of mice seems to be fairly rapid as shown by the disappearance of the drug within four hours. In mice sulphanilyl-benzamide reaches a moderately high concentration in the blood a half to one hour after administration, very similar to that produced by equimolecular proportions of sulphanilamide at the same interval after administration. The concentration of sulphanilyl-benzamide, however, tends to be maintained at a steadier level than is the case with sulphanilamide. From column 7, table II, it is evident that the percentage of conjugation in the case of sulphanilyl-benzamide is much lower than that in the case of sulphanilamide, when the drugs are administered in low dosage (0.1 mg./g.). In rabbits it was found that the drug did not reach as high a concentration in the blood as in mice, but the figure obtained indicated a fair degree of absorption.

(13) A comparative study of the anæsthetic and toxic action of 'trilene', trichlorethylene, chloroform and ether has been made on mice, guinea-pigs and rabbits.

In anæsthetic properties, 'trilene' and trichlorethylene showed certain characteristics common to both chloroform and ether, but muscular relaxation was almost as imperfect as with nitrous oxide.

Both 'trilene' and trichlorethylene are less toxic than chloroform, but ether proved to be safer than either of them. The anæsthetic dose of 'trilene' and trichlorethylene is slightly greater than that of chloroform but is much less than that of ether.

Favourable features of trichlorethylene anæsthesia are its rapidity of action, its analgesic effect and relative absence of early fatal accidents. Its chief disadvantage is its failure to produce complete muscular relaxation, and when this is required, resort must be had to supplementary ether anæsthesia. In view of observed toxic effects on the kidney and lung after administration of heavy doses of trichlorethylene, it would be injudicious in the present state of our knowledge to use trichlorethylene in cases where prolonged anæsthesia is required.

No difficulty was experienced by the authors in inducing anæsthesia in animals without the use of special apparatus.

(14) Although the incidence of malignant disease cannot be accurately estimated it appears to be sufficiently common in Ceylon to warrant further study.

Out of 10,880 consecutive biopsies 2,295 or 21.3 per cent showed evidence of malignant disease. The incidence of malignant tumours in biopsy material does not differ much from that recorded in India.

The primary carcinoma constituted 79.1 per cent of the malignant tumours and arose in 31 different sites. A high incidence of carcinoma in biopsy material was noticed in the following organs: the generative organs in both sexes (44.2 per cent), the cervix and penis alone (17.4 and 13.6 per cent respectively), the buccal cavity (15.1 per cent), skin (13.6 per cent) and the breast (9.6 per cent). The gastro-intestinal tract including the liver contributed only 3.4 per cent.

The predominating histological type was the squamous-cell carcinoma.

Although, as in other countries, females were seen to be more frequently affected, there was not much disparity in the sex incidence on account of the high incidence of cancer of the penis.

Our figures regarding racial incidence indicated only that people who were better informed of cancer sought hospital treatment at an early stage of the disease and did not wait till the carcinoma was inoperable or so obvious that a biopsy was rendered unnecessary.

The maximum incidence of carcinoma in both sexes appeared to be in the ten-year age-groups from 45 to 54, which is earlier than occurs in Japan, most European countries and the United States of America. The explanation for this is probably to be found in the fact that the expectation of life in the population of Ceylon is lower than that of the other countries.

Carcinomata occurring at certain primary sites have been discussed more fully. Some of the unusual features noticed were:—

- (a) A very high incidence of carcinoma of the cervix and penis in biopsy material.
- (b) The greater prevalence of certain types of tumours, such as the chorion epithelioma and the malignant melanoma, in Ceylon as compared with other countries.
- (c) The greater frequency of malignant changes found in ovarian cysts, thyroid and prostate glands.
- (d) The tendency for ovarian cancer to occur in women between 25 and 34 years.
- (e) The tendency for a large proportion of skin cancers to arise from chronic ulcers.

Malignant tumours of connective tissues (the sarcomata), lymphoid tissue and a group which, on account of its rarity, has been called 'special tumours' have been discussed. Sarcomata occurred in younger age-groups than the carcinomata and its incidence was found to correspond to that of Western countries and was much lower than that in India. Tumours of the lymphoid tissue also occurred in the young. The retinoblastoma was the most prevalent amongst the rare malignant tumours.

Malignant tumours in those under 20 years of age, which formed 5.2 per cent, have been discussed in respect to their incidence during infancy, childhood, pre-sexual and sexual periods. The more prevalent types characteristic of each of these periods have been indicated. The eye appeared to be more frequently involved than the other organs in this group.

Probable factors governing the causation of cancer in certain situations have been suggested. Our study has indicated that the controllable carcinogenic factor, *viz.*, continued irritation, operated on particular sites such as the cervix, oral cavity, penis and skin. This consideration brings a large proportion of cancers in Ceylon (59.7 per cent of the carcinomata in our series) under the group of preventable diseases.

The control of cancer in Ceylon does not appear to be so complex as in other countries, as a large proportion of the carcinomata (59.7 per cent in our series) arose in sites, which, on account of easy accessibility, were amenable to either surgical treatment or radium therapy. The difficulty, however, was the late arrival

of cases to hospitals as shown by this study. Only 161 of the 2,295 malignant tumours (7 per cent) could be regarded as early malignancy or pre-cancer.

The results that could be achieved by any form of therapeutic procedure is therefore necessarily limited. The general public should be enlightened regarding the intimate nature of the signs and symptoms which may mean cancer. The potential danger of neglecting a vaginal discharge, a sore on the penis, a wound or ulcer on the leg, a carious tooth or a polypus, and the relationship that these conditions bear to malignant disease should form a part of the educational propaganda in a campaign against cancer.

Whether a large proportion of sufferers from malignant disease are first seen by ayurvedic practitioners is a question which deserves investigation. While conducting an inquiry of this nature we must not fail to perfect our own organizations. Instruction in the early diagnosis of cancer should be an important feature in our medical curriculum and the necessary equipment for such diagnosis should be made available to every medical man.

Our hospital case records should be complete and should in every case include the reports of histological examinations. As the efficacy of any therapeutic procedure for malignant disease could only be judged by periodic examination of the patient, there should be a follow-up system whereby a cancer patient may be observed for at least 5 years after treatment.

These measures involve a great deal of perseverance, energy, patience and money. The sacrifice, however, will not be too great if we can be satisfied that a real gain has been made against a disease which has so stubbornly resisted the continued attack of sanitary science, bacteriology, chemistry, physics and even surgery.

(15) A detailed study of blood and bone-marrow changes in rabbits has been made after administering repeated small doses of manganese chloride.

In addition, to degenerative changes in the liver and spleen, toxic necrosis of the bone-marrow cells was observed, but of a lesser degree.

The hæmoglobin content of the blood and the peripheral blood cell counts were found unaltered, in spite of the damage to the bone marrow and fibrotic changes in the spleen.

Reparative fibrotic changes seen in the liver and the spleen were not in evidence in the bone marrow.

Experimental induction in rabbits, of a clinical condition similar to Banti's syndrome, with a toxic substance of the nature of manganese chloride is not possible, since only hepatic cirrhosis and fibrotic splenomegaly without anæmia were produced.

(16) The hæmatological findings based on a large number of observations in 59 *S. (M.) rhesus* monkeys are given. A comparison is made with similar findings in *M. mulatta* and *M. sinicus*.

(17) Figures to estimate stature from measurement of a single long bone in Punjabis have been worked out after examining the bones from 220 extremities. It is concluded that the stature can be estimated with the help of these figures to within an error of 1½ inches at the most, an error which is just over 2 per cent. A chart to serve as a ready reckoner of heights from the measurements of individual long bones has been prepared for use by medico-legal officers in the Punjab.

Cross-Infection by Dust

(From the *British Medical Journal*, i,
6th May, 1944, p. 624)

NEXT to chemotherapy the study of cross-infection has been perhaps the most notable feature of medical progress during the war, and it is a study in which this country has led the world. The proof that one patient has infected another often depends on the closest possible identification of the micro-organisms recovered from each of them, and is therefore possible in infections due to common species only when these

are divisible into many serological types. Unfortunately from the point of view of specific immunization, but very fortunately for the purposes of epidemiological study, there are two important species of which this is true. Just as the serological typing of the pneumococcus is a product almost entirely of work in the U.S.A., so that of hæmolytic streptococci—apart from the broader method of grouping devised by Lancefield—is entirely the work of an Englishman. No survey of this subject is complete without a tribute to the work of the late Frederick Griffith, to which the achievements of others in tracing the migrations of hæmolytic streptococci are entirely due. The knowledge so gained of cross-infection, particularly in surgical wards dealing with wounds and burns, and in E.N.T. and fever wards, has posed a problem to which the answers are still being found, though many have yet to be applied. It is an indication of the importance attached to this subject that two of the M.R.C. War Memoranda are devoted to it, no. 6 dealing solely with the problem as it affects surgical wards, and no. 11 published and reviewed in these columns only a few weeks ago, embracing cross-infection of all kinds.

There are two principal ways in which cross-infection can occur: through the air and by contact, either direct or mediate. The second of these routes embraces every kind of failure in aseptic technique, including some which were unsuspected until recently and unprovided for in usually accepted rules. By no means everyone yet appreciates the infectivity of a patient's skin at some distance from his wound, of apparently unsoiled outer dressings or of the outer surface of a soiled plaster, or the capacity of hæmolytic streptococci for survival on all manner of objects used by an infected patient. On the other hand, an even more striking fact brought fully to light only in the past three years is the degree and persistence of infection in ward dust. All observers who have studied this quantitatively agree in their findings that dust from wards where there are patients with hæmolytic streptococci infections may contain hundreds of thousands or even millions of these organisms per gramme. They are also known to survive in this medium for long periods; while a substantial number will certainly survive under favourable conditions for a month; a few survivors—in naturally infected dust kept in the dark have been observed by L. P. Garrod after a lapse of over six months. The production of such dust is still something of a mystery even to those best acquainted with it. It consists mainly, as does all domestic dust, of particles of wool or cotton, and many of these are evidently contaminated with infected wound exudate or throat secretion. However produced, it remains an obvious menace, accentuated whenever it is scattered into the atmosphere by bed-making or floor-sweeping. One important question which remains unanswered is how much cross-infection in the average ward is due to dust and how much to some form of contact. In other words, have we to concentrate on purifying the ward atmosphere or on improvement in aseptic and general nursing technique? This is by no means easy to answer, as may be gathered from a careful study recently made by Edward. This comprised quantitative bacteriological examinations of dust at intervals of a week for six months in two wards, one for E.N.T. and eye cases and the other a children's ward, together with regular swabbing of throats and any septic lesions in the patients and staff. The numerous hæmolytic streptococci recovered were typed, and the types found in the dust were usually those with which one or more patients were known to be infected. On the other hand, there sometimes appeared in dust a fresh type which had not been isolated from any patient, presumably having been introduced from without by a patient attending for a dressing. In spite of this very close method of observation, and of the occurrence of numerous cases of hospital infection, no conclusive evidence was obtained of its transmission by dust.

Perhaps the clearest evidence hitherto forthcoming of the proper apportionment of blame to dust and contagion respectively, at least in one type of ward, is to

be found in the paper by Joyce Wright, R. Cruickshank and W. Gunn in this issue of the *Journal*. There is, as is now well known, one method of dealing with the dust danger which can be applied anywhere, regardless of hospital structure or the absence of up-to-date cleaning facilities, and this is the use of oil to make dust particles sticky, so that they undergo agglutination on the floor instead of remaining easily dispersible in the air. This treatment was applied with the utmost thoroughness, not only to the floor—which alone was almost without effect—but to almost every fabric article in the ward, notably the bedclothes and the patient's garments. An identical ward, also accommodating patients with measles, was not so treated. In the oiled ward total counts of bacteria and hæmolytic streptococci in the air during bed-making and sweeping were reduced by about 91 and 98 per cent respectively, both from counts previously obtained in the same ward and those which continued to be obtained in the control. The incidence of infection by the Type 6 hæmolytic streptococcus then prevalent in both wards was only 18.6 per cent, whereas in the control it was 73.3 per cent, and the frequency of otitis media was 2.8 per cent, as against 14.3 per cent in the control. This is clear evidence that under these conditions dust is a major factor in cross-infection, and the demonstrated infectivity of various ward articles can account for only a small fraction of the troubles to which such wards are subject. Valuable as this evidence is, it should perhaps be accepted as applicable only to wards for infections confined to the respiratory tract. Where wounds are concerned, contact may possibly play a greater and dust a lesser part, although it is hard to believe, in view of these very definite findings, that dust can ever be unimportant.

This paper is one of three which deal with different aspects of the same subject. That the oiling of floor

thus be impregnated with any desired amount of oil, leaving a fluid from which no surplus oil has to be recovered. Cotton requires somewhat more complex treatment, but on the same principle. If, as seems probable, this process comes to be recognized as an essential safeguard in many hospital wards, these authors' instructions will no doubt be widely followed in the future.

Treatment of Cerebral Malaria

(From the *British Medical Journal*, ii, 5th August, 1944, p. 181)

Lieut.-Colonel J. M. Rogan, M.D., writes :—

DURING recent months certain contributions on malaria have appeared in the *Journal* which have apparently been written by authors with limited experience of this disease. Although these contributions have added little or nothing to existing knowledge, they have in the main been helpful to those who are encountering malaria for the first time. This cannot be said of the article by Surg. Lieut. Sneddon (*Journal*, 1943, 2, 814), reporting a fatal case of cerebral malaria, in which the commentary on treatment is seriously misleading.

DOSEAGE OF QUININE

The author records the administration of intravenous quinine in a dosage of 10 gr. daily, and comments that this dosage was higher than the 5 to 7 gr. daily advocated by Manson-Bahr (1942), leaving the impression with the reader that 10 gr. daily should be adequate for the treatment of cerebral malaria. It may be useful to present in tabular form the recommendations of various authorities on the optimum dosage of quinine in that disease.

Authority	Preparation	INITIAL DOSE		SUBSEQUENT DOSAGE INDICATED	
		Grains	Route	Amount	Route
Field (1938)	Quinine dihydrochlor.	7½	I.V.	10½ grains; up to total of 30 grains in 24 hours.	I.M.
Manson-Bahr (1940a) ..	" "	10½	I.M.	'Free and frequent administration of quinine.'	Not stated.
	" "	10	I.V.		
Manson-Bahr (1940b) ..	" "	15	"	Not stated	
Manson-Bahr (1942) ..	" "	5-7	"	5-7 grains daily	I.V.
Napier (1943)	Quinine dihydrobrom.	10	"	Repeat 10 grains a few hours later; intravenous therapy may be needed for 2 days.	"
Nocht and Mayer (1937) ..	Quinine dihydrochlor.	7½	I.M.	Not stated	..
	" "	7½-15			
Rogers and Megaw (1942) ..	" "	7½	I.V.	"Not more than 30 grains in 24 hours.	I.V.
Stitt (1942)	Quinine bimurate	10	"		

alone may be useful in living-rooms as distinct from hospital wards is evident from the interesting experiment made by Lieut.-Colonel Anderson and his colleagues in two Army barracks. Floor oiling in one of these was accompanied by a striking diminution in the frequency of respiratory infections, and the significance of the figures obtained seems unquestionable in view of the care evidently taken to provide an exact control, and to observe and record in both units according to the same plan. That those responsible for cleaning liked oiling as a system, apart from its benefit to health, is an encouraging fact. A third paper is by three members of the staff of the British Launderers' Research Association Laboratories, who were invited to study the oiling of fabrics with a view to devising an economical process which would be feasible in any laundry. In this they have well succeeded, since it appears that by adding a small amount of a cationic detergent the oil in an oil-in-water emulsion can be caused to be wholly absorbed by wool. Blankets can

It will be noted that the recommendations above are far from consistent. Though they may each have given satisfactory results in the particular conditions in which they were used, their diversity makes it difficult for the novice to decide on the correct line of treatment. In general it may be stated that the amount of treatment required will vary in inverse ratio to the amount of immunity possessed by the patient. Thus considerably large doses of quinine may be required for the majority of Europeans and Americans who usually possess little or no acquired immunity, than for patients living in endemic areas, who may possess partial immunity.

RECENT RECOMMENDATIONS

Since the outbreak of the present war large numbers of Allied troops with attendant medical services have been deployed in highly malarious areas, providing an unprecedented opportunity for the study of malaria in general and of its neurological complications in

particular. The following simple directions have been compiled from the most recent recommendations of the Allied forces on the treatment of cerebral malaria, and are founded on the experience gained before and during the present war. They are applicable to any case occurring in the adult male.

Drug of choice: Quinine dihydrochloride.

Route: Intravenous.

Rate of injection: Very slow. Maximum speed 1 minute per grain; optimum speed 2 to 4 minutes per grain.

Initial dose: 6 to 10 gr.

Dilution: Minimum 6 gr. in 10 c.cm.

Diluent: Distilled water or normal saline if 10 c.cm. is used. Normal or glucose saline for larger quantities.

Subsequent dosage: 6 gr. 4 to 6-hourly, not exceeding a total of 30 gr. in 24 hours, or 10 gr. 8-hourly, until recovery from coma occurs and satisfactory oral administration is possible.

Intramuscular mepracine as an adjuvant to intravenous quinine may give good results in the hands of those familiar with its use. I wish to emphasize the necessity for preserving with intravenous quinine in comatose cases even though the prognosis appears hopeless. This is well illustrated in a case reported by Whitehill (1943). Whitehill's patient was in coma for approximately 3½ days, excluding a lucid interval of 1½ days, and, although the coma was complicated by an acute malarial nephritis, recovery ensued after a total dosage of 75 gr. of intravenous quinine had been given.

POINTS FOR COMMENT

There are two other points in Surg. Lieut. Sneddon's article which are worthy of comment:

1. *Use of intravenous salines.*—A not infrequent terminal event in cerebral malaria is pulmonary oedema, and caution should always be exercised not to give more intravenous saline than is necessary, and to give it slowly. The administration of fluids through a Ryle's tube passed into the stomach and connected to a drip apparatus has been recommended by Lieut.-Colonel C. A. Ransome, I.A.M.C. (personal communication). It is advisable to nurse patients in a semi-recumbent position rather than dead flat, in order to prevent hypostatic congestion.

2. *Lumbar puncture.*—This should be carried out as a routine in coma. A certain proportion of cases of cerebral malaria suffer from cerebral oedema with a raised C.S.F. pressure, and, in these, improvement may follow the judicious removal of C.S.F. Further, in malarious areas cases of cerebrospinal meningitis may suffer simultaneously from malaria. The dual pathology may here easily be missed unless a lumbar puncture is carried out.

In conclusion I would like to express my emphatic concurrence in Surg. Lieut. Sneddon's statement that if treatment is to be successful it must be prompt. More than any other factor in the management of the case, the prognosis in cerebral malaria depends upon the speed with which the diagnosis is made and treatment instituted.

How to Interpret the W.R.

(From the *British Medical Journal*, i, 10th June, 1944, p. 801)

A positive W.R. carried out by a reliable pathologist is confirmatory evidence of syphilis if a patient has clear-cut signs of the disease. *In the absence of signs of syphilis no positive serum test, no matter by whom it is done, even if it is positive on a second specimen, in itself justifies institution of antisyphilitic treatment.* Quite a number of pathological conditions—mostly tropical diseases and therefore not likely to be met with in this country—may be responsible for false positive reactions. But such conditions as glandular fever,

scarlet fever, pneumonia, late tuberculosis, diabetes mellitus, enteric fever, and malignant tumour—to mention only a few—have been incriminated from time to time. Recent vaccination also has been shown to be a cause. In addition there are people, very few it is true, whose sera appear to be 'labile' in that they give false positive reactions without apparent reason.

In most of the above conditions the W.R. remains positive only for a comparatively short time, and tests repeated over a period of three months will usually show a weakening of the reaction or return to negativity. As a general rule, therefore, one should not diagnose syphilis on serum reactions alone unless they remain positive for at least three months. Meantime, a complete clinical examination of the patient should be carried out, including radiography of the heart and great vessels and examination of the cerebrospinal fluid.

The term 'weak positive' should never be used. A 'doubtful' reaction is one which is neither positive nor negative, and, except in an established case of syphilis should merely serve as an indication for further investigation, both clinical and serological. A negative reaction does not exclude syphilis. The serum of a syphilitic patient gives a negative reaction in the first few days after the appearance of the sore, and not infrequently in the late stages of syphilis and especially in tabes dorsalis, not to say in syphilis which has been insufficiently treated.

Intestinal Amœbiasis

(From the *Lancet*, i, 17th June, 1944, p. 793)

AMŒBIC dysentery, or more properly intestinal amœbiasis, flourishes when sanitation is defective and especially in warm countries where defective sanitation is associated with a prolific fly population. Large numbers of men are returning to this country from such areas and many of them are likely to be harbouring *Entamoeba histolytica*. Some of these men have had frank bacillary dysentery; others have had clinically obvious attacks of amœbic dysentery. Yet others may give no history of such attacks but still be infected with *E. histolytica*; they may or may not develop clinical attacks of the disease later, but in either case they remain infected for many years, and, even more important, they are infective to others. It is these persons, passing cysts, who are responsible for the maintenance and spread of the infection in man. Such are responsible for some of the autochthonous cases of amœbic dysentery encountered from time to time in the United Kingdom among the civil population. It is salutary to recall that in 1917 examination of the stools of 206 men called to the colours, who had not previously been out of Great Britain, showed that 3.9 per cent harboured *E. histolytica*. This figure was based on a single stool examination, and if three or more specimens had been examined from each case the figure would probably have been much higher. None of these men gave any history of dysenteric attacks; nevertheless, feeding experiments on kittens with cysts from one of the cases showed them to be of an actively pathogenic type.

The apparent absence of pathogenicity of the parasite in some human cases and its modification in others has been the subject of much speculation. The asymptomatic carrier of *E. histolytica*, or as he is less happily called, the 'cyst passer', invariably has lesions in the mucosa and submucosa of the large bowel, but these are insufficient in number and extent to give rise to gross clinical signs. Faust, discussing the variable effects of amœbiasis on the host, suggests that if but a small number of viable cysts are swallowed the scanty parasites emerging from them have little opportunity of coming into contact with the mucosa of the large bowel and infection may not result at all; irritability of the bowel with rapid passage of its contents may similarly prevent the amœbic becoming established. Faust expresses the view that people in mildly endemic

areas are probably often exposed to small infecting doses of viable cysts but these may be unsuccessful in colonizing the bowel. Frequent exposure to a large number of cysts, on the other hand, affords suitable conditions for the development of heavy infections among a population. There is some experimental evidence that strains of *E. histolytica* do vary in virulence, but no evidence that any are non-pathogenic. Virulence of a strain may be enhanced experimentally in animals by rapid subpassage, and Faust holds that this may explain the rapidity with which an epidemic of the disease in man may develop once heavy initial infection has been provided. Nevertheless, in addition to being a qualitative disease, dependent on the virulence of the infecting strain, amoebic dysentery is a quantitative disease. Its clinical manifestations are proportional to the levels in the gut at which the amoebic lesions occur, their numbers and extent, and the depths of their penetration into the gut wall. In the case of a light infection established well down in the large bowel, clinical evidence of the infection would be insignificant; but where there is a more massive infection higher up, in the caecum, then amoebae from the lesions are carried down in the bowel and colonize its whole length; in such cases frank dysentery results from the increase in number and extent of the lesions. There is no evidence of racial or group tolerance to this parasite but long infection tends to establish a host-parasite equilibrium and clinical manifestations of the parasitization diminish. Commonly overlooked results of an infestation are appendicitis and a general colonic upset, often associated with digestive disturbances akin to those attributable to a peptic ulcer. The complication of embolic spread of the parasites into the portal circulation from the gut is only too obvious when a definite amoebic liver abscess develops; but there is reason to believe that not every case where such spread occurs terminates with a frank abscess. The liver tissue seems to possess some anti-amoebic action; thus in experimental gut infections in dogs fresh raw liver, or freshly expressed liver juice, will sometimes act as an amoebistatic or even an amoebicidal agent when given either by mouth or as a high retention enema. Parenteral injections of filtered freshly extracted liver juice or commercial liver extracts are ineffectual.

Though steady progress has been made in the development of new drugs for the treatment of amoebiasis, the position is not yet satisfactory. No single drug will eradicate more than a certain proportion of infections, and it is usual to combine a number of drugs in an endeavour to obtain sterilization. Even then there is no combination of drugs which provides a guaranteed cure, and there is abundant need to explore new fields of therapy. Emetine hydrochloride is the only known satisfactory drug in the treatment of amoebic hepatitis and amoebic liver abscess. Its efficacy in amoebiasis of the gut is limited to control of the acute symptoms. This is a point which deserves emphasis, for there is an unwarranted tendency to push the drug to the limit of tolerance and repeat the procedure unduly. A few daily intramuscular injections of emetine hydrochloride in doses of gr. 1 will achieve as much as bigger or more protracted dosage—arrest of the acute attack. There can be no justification for the 100–200 injections of emetine which some sufferers from the disease have endured. The end-result of unnecessary and excessive emetine administration may well be the development of an infection resistant to all drug therapy and evidence of emetine poisoning. After the attack has been brought to an end by judicious and conservative dosage, sterilization of the intestinal infection should always be attempted by the concerted use, over a period, of a variety of drugs among which chiniofon retention enemas, together with an arsenical preparation such as acetarsol or carbarsone and an emetine compound such as emetine-bismuth-iodide or 'Auremetine' by mouth, usually find a place in this country. The prospects of radical cure are good, particularly if ineffective over-treatment has not previously been indulged in.

Hepatitis After Transfusion

(From the *British Medical Journal*, ii, 26th August, 1944, p. 279)

TRANSFUSION of whole blood has never been a procedure entirely free from risks. Reported mortality figures from the operation have varied in different series from 0.1 to 1 per cent. Death has usually been due to renal failure after hæmolytic crises or to heart failure from circulatory overloading. Less severe reactions—hæmolytic, pyrogenic, and allergic—and non-fatal vascular accidents also occur. The administration of blood products—plasma and serum—is not attended, other than in exceptional circumstances, by hæmolytic reactions; but the other above-mentioned dangers remain. Another transfusion hazard is now being reported and must be seriously considered. Hepatitis is occurring after the use of certain batches of human serum and plasma. This danger was anticipated by the Ministry of Health, whose medical officers a year ago published a memorandum on this 'homologous serum jaundice'. Up till then the condition had been recognized chiefly after yellow-fever vaccination, the virus being suspended in human serum. Such reports had come from this country, South America, and the U.S.A. Hepatitis was also known to occur after the injection of serum from a measles convalescent, and, latterly, also after the injection of plasma from a mumps convalescent. In the last year the condition has been seen, and in some cases reported, after transfusion of serum and plasma. Bradley, Loutit, and Maunsell make a further contribution to this story in our present issue.

In one or two instances jaundice after transfusion of blood alone has been seen. It is, however, more difficult to be certain of the diagnosis in such cases. Batches of plasma and serum can be incriminated because multiple cases occur after their use; more or less homogeneous material has been given to many recipients. This does not obtain with whole-blood transfusion, which is a much more individual affair. Unless a single donor's blood on repeated occasions results in jaundice of the recipient, it is impossible categorically to aver that his blood carries a hepatotoxic agent; such a donor has not yet been reported. If he does exist—and he probably does—then his plasma or serum could easily make a large pool icterogenic. Very small quantities even of pooled material are effective, though the dose and route of administration seem to bear no relation to the severity of the resulting hepatitis. This homologous serum jaundice is probably closely related to post-arsphenamine jaundice, also very prevalent at present. Contamination of syringes with human material from previous use has been suggested as the cause of this. Its relation to infective hepatitis is less clear. There is some evidence that an attack of homologous serum jaundice or post-arsphenamine jaundice confers no immunity to infective hepatitis, and vice versa. The cause of homologous serum jaundice is therefore unknown. A virus aetiology has been postulated: MacCallum and Bauer conclude from their experiments that the evidence 'is not inconsistent with the view that the agent is capable of multiplying in tissue culture'.

Although series of cases are now being published, the cause of jaundice must have been misinterpreted in many more. The latent period before the onset of jaundice and the accompanying symptoms is long—40 to 160 days; thus the connection with previous transfusion may be missed. The clinical picture and the biochemical findings are usually indistinguishable from those of infective hepatitis. Most of the cases occurring may well be masquerading under this diagnosis. Although like infective hepatitis, the condition is usually mild and of short duration, there is an impression that the mortality is higher; for example, among about 200 probable cases, not including yellow-fever-vaccine jaundice, there have been 13 deaths. In most of the transfusion cases, in contradistinction to the

vaccine and convalescent-serum cases, it has been difficult or impossible to ascertain the batch of serum or plasma responsible for the condition. This is mainly because the batch and index numbers of the materials used have not been entered on the patient's case sheet. As yet, human serum and plasma processed for transfusion are not covered by the Therapeutic Substances Act, the terms of which would require such details to be recorded. As soon as the war is over steps will have to be taken to bring such transfusion materials within the scope of the Act. In the meanwhile much can be done to prevent the widespread distribution of incriminated batches. Due caution should be observed as regards the transfusion of serum or plasma; if available, blood should be given rather than serum or plasma, and unless there are strong indications for the latter (e.g. hæmoconcentration). So far as possible any one case should be transfused with serum or plasma from one batch only; careful records of batch and index numbers of materials given should be kept voluntarily by medical officers performing transfusions; and a follow-up should be made for at least 4 months on all cases transfused. The appointment for each hospital or group of hospitals of a full-time transfusion officer, whose duties would include the keeping of the records and the supervision of the follow-up, would facilitate this process. When hepatitis cases are discovered through the follow-up they should be notified to the Regional Transfusion Officer, together with the index numbers of the blood, serum, or plasma given. In this way the Regional Transfusion Officer would be able to arrange for the removal from circulation of ieterogenic batches.

Prevention of Jaundice Resulting From Antisyphilitic Treatment

By M. H. SALAMAN

D. I. WILLIAMS

A. J. KING

and,

C. S. NICOL

(Abstracted from the *Lancet*, ii, 1st July, 1944, p. 7)

THE incidence of jaundice in patients receiving arsenic for syphilis was greatly reduced by a technique of injection designed to eliminate possible transference of infection from patient to patient.

In 67 men treated by the ordinary technique for 120 days the incidence of jaundice was 37 per cent and in 56 of those treated for 180 days it was 68 per cent. Of 36 men treated by the new technique for 120 days only 1 developed jaundice. Similarly in 18 treated for 180 days only 1 was affected.

Impetigo Contagiosa Treated With Microcrystalline Sulphathiazole

By J. W. BIGGER

and

G. A. HODGSON

(Abstracted from the *Lancet*, ii, 15th July, 1944, p. 78)

OF 50 cases of impetigo contagiosa treated with microcrystalline sulphathiazole, 48 were cured in an average of 5.3 days. Of 25 treated with sulphathiazole, 23 were cured in an average of 6.5 days.

On the application of microcrystalline sulphathiazole oozing usually ceased within one or two days and epithelium rapidly regenerated. But cure was sometimes delayed by the appearance of fresh lesions. The organisms found in the lesions seldom disappeared before healing was well advanced.

Individual lesions were more rapidly healed, and the time required for the cure of the disease was shorter,

with microcrystalline sulphathiazole than with any treatment previously tried.

Only one patient treated with microcrystalline sulphathiazole developed sensitivity.

Jaundice in Syphilitics

(From the *Lancet*, ii, 15th July, 1944, p. 91)

By HUGH CLIME

There is now much evidence that the occurrence of jaundice in syphilitics is due to an infective agent which may be conveyed from case to case by means of the syringes used in treatment, if these are inadequately sterilized.

The clinic with which I am associated is a small one, and we have always been able to sterilize our syringes between cases by boiling. It is therefore worthy of note that only 4 cases of jaundice occurred in 346 male cases of syphilis treated during the past four and a half years, though 11 of these had had attacks before commencing treatment here. Of the 4 cases, 2 (one soldier and one merchant seaman) showed signs of jaundice on their first attendance. The other cases occurred in two men who had been sent to another hospital for a course of inductopyrexia. They were there many weeks and were discharged about the same time. One developed jaundice within six weeks and the other within three months of discharge from the institution. No cases of jaundice occurred among regular attenders of this clinic in the ensuing six months.

Such observations lend practical support to the view that a considerable reduction in the amount of post-arsenical jaundice could be obtained by careful attention to injection technique and sterilization of syringes.

The Treatment of Filariasis (*Wuchereria bancrofti*) With Lithium Antimony Thiomalate

By H. W. BROWN, M.D.

(Abstracted from *Journal of the American Medical Association*, Vol. CXXV, 5th August, 1944, p. 952)

1. LITHIUM antimony thiomalate, a compound given intramuscularly to a series of filaria-infected patients, reduced their microfilaria count 85 to 100 per cent. This reduction was maintained for four to five months after the completion of treatment and means presumably that a corresponding number of the adult worms were killed. One patient failed to respond to treatment, and there was no reduction in his microfilaria count.

2. No reduction in size of enlarged lymph glands or one enlarged scrotum could be detected four to five months after the completion of treatment. One patient noted a pronounced improvement in his inguinal distress on exercise following treatment.

3. The patient's history and physical examination failed to reveal any pathologic changes due to the death of the adult worms of microfilaria.

4. The toxic manifestations due to lithium antimony thiomalate of vomiting, joint pain, slight fever and rash are not considered sufficient to preclude its continued trial in filariasis.

Intravenous Fluids

(From the *Lancet*, i, 6th May, 1944, p. 601)

MANY substances are now used for intravenous infusion, and much is written on the relative merits of blood, blood substitutes, protein derivatives and crystalloid solutions. In deciding which of them to employ, one must be clear about the object in view. The purpose of the infusion may be:—

- (1) Supply of fluid or nourishment to the tissues.
- (2) Restoration of the volume of blood in circulation.

(3) Reinforcement of the oxygen-carrying power of the blood.

(4) Contribution of special elements, such as leucocytes, clotting factors and antibodies.

Intravenous infusion of isotonic saline and dextrose solutions has long been used to bring fluid and food to thirsty and hungry tissues. Often patients depend for a time entirely on such support, and we now know something of the principles governing their requirements of fluid, chloride and dextrose. Giblin's recent account of abdominal surgery in the Alamein campaign is a striking tribute to the success of alimentary rest during the four or five days following operation, during which time the patient is hydrated entirely by vein and his comfort assured by continuous gastric suction. More ambitious is the attempt to supply protein to the under-nourished by the intravenous route. Whipple and his colleagues have shown experimentally that injection of suitable protein can provide all that is necessary for protein metabolism, enabling the body to increase its plasma protein and to form new haemoglobin, and they consider it valuable for states associated with deficient nitrogen intake or with tissue injury accompanied by nitrogen loss—including hæmorrhage, burns and major operations. Hydrolysates of casein, and Rose's growth mixture of ten crystalline amino-acids, appear to be efficient for this purpose, while Elman has used human plasma.

When an injury has caused loss of blood or plasma, or both, the main object of a transfusion is to restore blood-volume. For this purpose crystalloid solutions such as physiological saline have only a fleeting value, for they are rapidly exerted. To secure any permanent restoration of blood-volume one must inject substances likely to stay in the blood-vessels and great efforts have been made to produce a stable efficient volume-restoring fluid which is innocuous, is well retained, and is finally metabolized usefully. Plasma and serum—safest in dry form—have been universally acclaimed as highly satisfactory, and they have the additional advantage of supplying natural protein for metabolism; but there are two objections to them. The first, especially cogent in war-time, is that the bulk of bottles to be carried is never less than that of the blood lost. The brilliant work of Cohn and his associates may get us over this difficulty, for they have produced from human blood a crystalline albumin fraction, efficient in amounts as small as 25 c.cm., which is now undergoing extensive trial; but it is not yet certain whether this concentrate will do its work as such or whether equivalent fluid will not have to be provided at the same time, especially when the state of hydration is low. The second and more serious objection is that plasma and serum have to be got from human donors. Could this burden be transferred to the animal world, the problem of the volume-restoring blood substitute would be simple; but unfortunately natural bovine serum is not tolerated by man, and Heyl and his colleagues can make no statement regarding the safety even of its crystallized albumin fraction. A further line of approach is opened up by the work of Ronald Edwards with 'despeciated' bovine serum. Yet here again the originator concludes that final judgment must await the results of more detailed studies in a wider field than the 26 cases so far investigated. The ingenuity of the Germans has naturally turned to the invention of a synthetic substitute (known under the trade name of 'Periston'), but its composition was not published till their experience had called forth the sincerest form of flattery to the Allies—namely, the production of their own dried serum. At present the most promising source of non-human material seems to be pure animal gelatin in the form of isinglass, which has proved safe and effective: the raw material is virtually unlimited; it can be made into a standard product on a large scale without undue expense; and it is said to have some value in protein metabolism. Clearly, however, there is not yet enough evidence to justify a change of policy by any of the countries now devoting their resources to the production of human plasma or serum—safe and well-tried products that have the double

advantage of restoring blood-volume and contributing to protein nutrition.

The body is remarkably tolerant of big reductions in the oxygen-carrying power of the blood, provided the efficiency of the circulation is maintained. Even after serious loss of blood, therefore, infusion of plasma may at first be almost as useful as infusion of whole blood. Restoration of hæmoglobin is nevertheless important to full recovery, and Ogilvie reports from Africa that 'given a free choice and an abundant supply of both transfusion officers tend to use 2½ pints of blood to 1 pint of plasma'; to which he adds his opinion that if a man has lost 4 pints of blood he will probably die unless he receives at least 1 pint of whole blood in return. For the treatment of simple anæmia of hæmorrhage stored blood which has been cleanly and properly taken, and immediately and accurately refrigerated, is almost the equivalent of fresh blood, so long as the storage period does not exceed 14 days; indeed Loutit and Mollison claim that with an acid citrate anticoagulant this period may be extended even to 28 days. Stored blood, however, carries a heavy risk unless carefully tended. Mollison has shown that intravascular hæmolysis may take place in patients transfused with aged stored blood, with blood stored at an unsuitable temperature, or with blood stored in a solution containing no glucose, and the use of infected stored blood may cause fatalities with symptoms closely simulating intravascular hæmolysis. The caretaker of a blood bank has a responsible post, especially under field conditions. When the purpose of the transfusion is merely to facilitate transport of oxygen through the body it is useful to use packed cells, as was found by Watson. But in cases where the aim is to supply blood elements such as leucocytes or clotting factors, it is well, as the Edinburgh school have demonstrated, to use fresh blood, and there is considerable support for the opinion of Julian Smith that direct transfusion of fresh blood gives the best results in many of the blood dyscrasias.

In the immediate future we may have reason to be grateful to those who have overcome great obstacles to make intravenous infusion and transfusion part of the ordinary treatment of our wounded. As Professor Wilson shows on our opening page, there are failures as well as successes; but the work of the blood-transfusion services, both in the field and at home, has fully justified the hopes of the hundreds of thousands of people who have given their blood.

Journal of the Malaria Institute of India

5, No. 3, June 1944

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The authors' summaries or abstracts of the above papers are given below:—

MALARIA INVESTIGATIONS IN NORTH KANARA

A malaria survey of North Kanara district, Bombay Presidency, was carried out during the period of May 1942 to May 1943 by a research unit from the Malaria Institute of India. Malaria is prevalent in an endemic form throughout the district, though patches of low endemicity are present. In the ghat section the disease is hyperendemic. The coastal area is comparatively free. The chief malaria season extends from October to June, but transmission may occur during any month in the year. *A. fluviatilis* is the only malaria carrier of importance in this area. There is no evidence that any other species plays any part in transmission. The infection rate was 11 per cent, somewhat lower than that recorded in the Wynad and Nilgiris foothills for the same species. The bionomics of this species have been discussed. Sixty-four per cent of *A. fluviatilis* whose gut contents gave positive results with the precipitin test were found to have fed on human blood. Control measures in relation to the vector species have been formulated. Since this mosquito selects human habitations for its daytime resting place, the spray-killing of adult mosquitoes with pyrethrum insecticides should prove of special value in this area.

EPIDEMIOLOGY OF MALARIA IN THE NIZAMSAGAR AYACUT AREA, NIZAMABAD DISTRICT, HYDERABAD STATE

An account is given of the malarial conditions and control measures adopted in Nizamabad district, Hyderabad State. Prior to the introduction of canal irrigation under the Nizamsagar project, malaria was not an important problem in the district. The incidence of the disease has greatly increased since the scheme was put into operation. The increase in malaria is attributed to various defects in the irrigation system, e.g. inadequate provision for drainage, failure to maintain distributaries and channels, defective sluice gates, excavation of borrowpits, etc. The spread of the disease was further favoured by the introduction of large numbers of labourers who acted as reservoirs of infection. The chief malaria carrier is *A. fluviatilis*. It is considered probable that *A. culicifacies* also plays some part in transmission. Out of 865 blood films examined 19.0 per cent contained parasites of *P. malariae*, 16.4 per cent *P. vivax* and 12.7 per cent *P. falciparum*. A malaria control scheme was inaugurated in 1942. The chief measures adopted are the spray-killing of adult mosquitoes with pyrethrum insecticides, the application of oil and paris green to breeding places and various minor levelling and drainage operations. Mass prophylactic treatment with quinine is carried out in certain hyperendemic villages.

THE FORECASTING OF EPIDEMIC MALARIA IN THE PUNJAB

The accuracy attained by the method used for the forecasting of epidemic malaria in the Punjab has been statistically evaluated and it has been demonstrated to have been successful in predicting areas where epidemics are likely to occur. A consideration of the facts set out justifies the conclusion that malaria epidemics can be predicted with considerable precision, inasmuch as isolated small areas likely to experience malaria epidemics can be specified.

The method which has so far been adopted would seem to suffer from the defect that it involves a personal factor. The basic data used for formulating the forecast, however, are all stated numerically. It should, therefore, be possible to eliminate the personal factor altogether by replacing it by the use of modern statistical methods of regression and trends.

THE EXPERIMENTAL TRANSMISSION OF QUARTAN MALARIA BY *A. culicifacies* GILES

The transmission of *P. malariae* Lav. by experimentally infected *A. culicifacies* Giles, reared in the laboratory is described. *A. culicifacies* is shown to be

a very efficient vector of quartan malaria. The infectivity of the gametocytes of *P. malariae*, which appears to be a more important factor in the infection of *A. culicifacies* than the susceptibility of this mosquito to the parasite, was found to be highest during the cold weather, as exemplified by conditions in Calcutta.

The extrinsic incubation period of *P. malariae* in *A. culicifacies* was 14 days at 80°F. and 19 to 22 days at 70°F. The intrinsic incubation period of *P. malariae* was 30 days, and the clinical incubation period was 36 days. Observations on periodicity, rate of segmentation, development of resistance and gametocyte production in the untreated infection are recorded. The presence of a really efficient vector species of anopheles and a climate characterized by high atmospheric humidity for long periods are two of the most important factors in the distribution of quartan malaria.

OBSERVATIONS ON THE INFLUENCE OF ATMOSPHERIC TEMPERATURE AND HUMIDITY ON THE INFECTIVITY OF *A. culicifacies* GILES

An account is given of unfinished work on the influence of atmospheric temperature and humidity on the infectivity of *A. culicifacies*. Lowering of temperature within the range 94°F. to 70°F., particularly when combined with an increase in relative humidity, enhances the period of survival of *A. culicifacies*. This species appears to be adversely affected by mean temperatures below 60°F. and humidities below 60 per cent. The upper limiting value of temperature for development of Indian strains of *P. vivax* and *P. falciparum* in *A. culicifacies* lies between 90°F. and 94°F. The optimum range of temperature for development of the parasites and transmission is from 70°F. to 86°F.; provided humidity is favourable for survival of *A. culicifacies* a relative humidity of 50 per cent does not appear to be entirely inimical. The lower limiting values of temperature for development of the parasites in *A. culicifacies* have not been determined, though *P. malariae* was not observed to develop at all at a mean temperature of 59.6°F. whereas oöcysts of *P. vivax* and *P. falciparum* were encountered under similar conditions. The extrinsic incubation period of the parasites varies from 7 days (*P. vivax*) at 86°F. to 19 days (*P. malariae*) at 70°F. The natural seasonal infectivity of *A. culicifacies* is briefly examined in the light of the experimental findings.

ON A NEW SPECIES OF THE SUBGENUS *Lophoceratomyia* THEOBALD 1905 (DIPTERA CULICIDÆ)

The male and female of a new species of *Culex* namely *C. (Lophoceratomyia) parainfantulus* are described in detail. This species is allied to *C. (L.) minutissimus* Theobald and *C. (L.) infantulus* Edwards. The three species differ from one another mainly in the structure of the male hypopygium. The position and appearance of the phallosome processes in the three species are quite unlike those found in other mosquitoes of the genus *Culex*.

ATEBRIN AND PLASMOQUINE IN THE TREATMENT OF BENIGN TERTIAN MALARIA

The febrifuge effects of atebriin-plasmoquine treatment (A.P.) and quinine-plasmoquine treatment (Q.P.) are approximately the same. Splenic reduction—slight bias in favour of A.P. Vomiting at commencement of attack fades more rapidly with A.P. than with Q.P. The latter may actually cause vomiting. Relapse rates are definitely lower with A.P. than with Q.P. Relapses are less frequent with a treatment of atebriin 7 days, plasmoquine 5 days, than with atebriin 5 days, plasmoquine 5 days. Average period of disappearance of parasites from the peripheral blood is 2 days after A.P. and 2.7 days after Q.P. The ultimate hæmoglobin content of the blood is several degrees higher after A.P. than after Q.P. A.P. thus appears to be established as superior to Q.P. in the treatment of *P. vivax* infections. All treatments tested were more effective in preventing relapses during a mild than during a severe epidemic. The results appear to indicate that the more severe is the attack of malaria the greater is the resulting immunity.

***P. tenue* FORMS AND 'BAND' FORMS OF *P. vivax* SEEN IN CEYLON DURING THE EPIDEMIC OF 1943**

In the course of routine blood examinations of outdoor dispensary fever cases in Ceylon, three films containing parasites resembling *P. tenue* Stephens were encountered. In two of these, half the parasites seen had the appearance of typical *P. falciparum* rings; the other half were characteristic *tenue* forms. No gametocytes were observed in either films. In the third film about one-tenth of the total number of parasites seen were *P. tenue* forms. Gametocytes of *P. falciparum* were fairly numerous. The infected blood cells in all cases were of normal size and shape. Neither pigment nor Stephens and Christophers' nor Maurer's dots were present in any of the films. A film containing parasites of *P. vivax* showing band forms is also described. The infection is described as a heavy one, with one or two parasites in each field. The band forms were scattered throughout the film, mingled with typical *P. vivax* forms. The infected cells containing the band forms were definitely enlarged and in several instances Schüffner's dots were present.

The Changes in Operative Gynæcology During the Last Quarter-Century

By L. E. PHANEUF, M.D., S.C.D.

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXVI, 16th September, 1944, p. 139)

THE last quarter of a century has shown significant improvement in surgical technique, with emphasis on careful dissection and ligation of individual vessels with fine material rather than mass ligation of tissues. The treatment of carcinoma of the cervix has changed from surgery to irradiation with the return to the radical pelvic operation by a few gynæcologists in early cases and good surgical risks. Carcinoma of the uterine corpus and fundus has remained a surgical lesion, surgery, however, having been complemented by irradiation. Improvement in the operation of myomectomy has resulted in more conservative management of these lesions in the young; supravaginal hysterectomy still remains the common method in use, while an increasing number of gynæcologists have turned to panhysterectomy as a prophylactic means against carcinoma of the cervical stump. Vaginal hysterectomy has been reborn and improved and has now become a commonplace procedure. The increased number of surgical vesicovaginal fistulas has been responsible for the elaboration of new techniques in the cure of this lesion. Trachelorrhaphy and amputation of the cervix are less frequently done, these having been replaced in many cases by cauterization and electrocoagulation. A significant advance has been made in the surgical treatment of uterine prolapse, cystocele and rectocele through better anatomic understanding of these lesions and by reconstructing the deficient supports through the vagina rather than by depending on abdominal suspension or fixation of the uterus. Pelvic inflammatory disease has been handled more and more by conservative methods, and the sulphonamide drugs seem to show great promise in lessening and eradicating this condition. Ovarian tumours have been better classified, the rare tumours have been discovered, the tendency of malignant changes in these neoplasms has been emphasized and their early ablation has been strongly advised.

New Rapid Method of Intubation With the Miller-Abbott Tube

By F. L. HARRIS

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXV, 15th July, 1944, p. 784)

Liquid metallic mercury in amounts of from 4 to 8 c.c. has been injected into the rubber bag of the Miller-Abbott tube to facilitate a more rapid and certain intubation.

In a series of 19 consecutive cases of obstruction of the small bowel the Miller-Abbott tube has been quickly and successfully introduced with the aid of this new technique.

It appears that the weight of mercury itself may carry the tube into the small bowel without the necessity of air inflation of the rubber bag.

Clinical and experimental work is contemplated with a new type of single lumen, mercury weighted, intestinal tube.

Clinical Use of Oral Thermometers

By N. DE NOSAQUO *et al.*

(Abstracted from the *Journal of Laboratory and Clinical Medicine*, Vol. XXIX, February 1944, p. 179)

1. THE character of the rise of the mercury column in an oral thermometer under clinical conditions is different from that under laboratory conditions.

2. In this study, thermometers marked with specific time designations '1 minute', '½ minute', and '60 seconds' were found to require about the same length of time for the instrument to reach equilibrium and thermometers with no time designations.

3. Three minutes should be the minimum time interval allotted for an oral thermometer to reach equilibrium under ordinary conditions of use.

Reviews

MEDICAL DISEASES OF WAR.—By Sir Arthur Hurst, M.A., D.M. (Oxon.), F.R.C.P. Fourth Edition. 1944. Pp. v plus 511. Edward Arnold and Co., London. Price, 21s.

IN this edition of this well-known book, the chapters on infective jaundice and infective hepatitis and the sections on sciatica and the treatment of bacillary dysentery have been re-written, and considerable alterations have been made in other sections of the book.

SALTS AND THEIR REACTIONS.—By Leonard Dobbin, Ph.D., and John E. Mackenzie, O.B.E., D.Sc. Seventh Edition. 1944. Pp. ix plus 246. E. and S. Livingstone Ltd., Edinburgh. Price, 8s. 6d.

THIS book is now in its seventh edition. In the preface it is stated that this book is written to provide practical instruction regarding the properties of the metals, oxides, hydroxides, acidic and metallic radicals, upon which the general chemical knowledge of the medical student is based, and to introduce him to the laws of chemical combination by the performance of simple gravimetric and volumetric experiments. The book is a good one and admirably fulfils its purpose.

THE BRITISH ENCYCLOPÆDIA OF MEDICAL PRACTICE: MEDICAL PROGRESS, 1943.—By Sir Humphry Rolleston, Bt., G.C.V.O., K.C.B., M.D., D.Sc., F.R.C.S., D.C.L., LL.D. Pp. iv plus 382 plus 29. Butterworth and Co. (Publishers) Ltd., London. Price, Rs. 26

THIS volume includes critical surveys of recent work on the following subjects:—

General medicine; General surgery; Obstetrics and gynæcology; Diseases of the blood-forming organs; Blood transfusion, recent developments; Diabetes mellitus; Ear, nose and throat diseases; Gastro-intestinal disorders; Infectious fevers; Lungs, pleura and mediastinum diseases; Mental diseases, nephritis and nephrosis; Nervous diseases; Ophthalmology; Tropical medicine; Venereal diseases.

There is also an article on recent developments in drug therapy and abstracts of recent literature on many points. Here and there among the abstracts are editorial comments which are interesting and valuable. The paper, printing and get-up are excellent.

THE BRITISH ENCYCLOPÆDIA OF MEDICAL PRACTICE: MEDICAL PROGRESS, 1944.—By Sir Humphry Rolleston, Bt., G.C.V.O., K.C.B., M.D., D.Sc., F.R.C.S., D.C.L., LL.D. Pp. iv plus 411 plus 126. Butterworth and Co. (Publishers) Ltd., London. Price, Rs. 37-8

THE general plan of the Annual Medical Progress Volume to the British Encyclopædia of Medical Practice has been followed in this, the fifth of such volumes. The first part of this volume contains a series of critical surveys of the following branches of medicine:—

Public health in the present war; Surgery; Obstetrics and gynaecology; Alimentary tract diseases; Bacteriology; Endocrinology; Acute infective diseases; Diseases of the lungs; Mental diseases; The autonomic nervous system; Neurology; Diseases of the prostate gland and bladder; Tropical medicine; Venereal diseases.

The second part discusses the recent developments in drug therapy and the third part gives abstracts. Much care has been bestowed on the selection of the abstracts. A cumulative index to all previous annual volumes to the encyclopædia and therefore covering the period 1939-44 is included at the end of this volume.

ESSENTIALS OF SYPHILOLOGY.—By Rudolph H. Kampmeier, A.B., M.D. Pp. xvi plus 518. Macmillan and Co., Ltd., London. Price, 25s.

THIS new book is by the Associate Professor of Medicine, Vanderbilt University School of Medicine, and officer in charge of the syphilis clinic. It is intended to provide a brief text on syphilis for the medical practitioner and the medical student. The author writes apologetically about the brevity of the book and thinks that he may be charged with superficiality; but its pages number over 500. Moreover, we do not think the charge of superficiality can be maintained if it is remembered that this book is not for the specialist on the subject. The teaching of the book is along generally accepted and sound lines and stress is laid upon the public health aspects of the problem. The book is excellently printed and produced.

J. L.

STUDIES ON IMMUNIZATION, SECOND SERIES, IV.—By Sir Almroth E. Wright, M.D., F.R.S. William Heinemann Medical Books Ltd., London. Pp. 256. Price, 25s.

THIS book is the fourth volume of the second series of the collected researches of the author from the Inoculation Department of St. Mary's Hospital, London. It contains nine papers published between 1910 and 1943. The subject covered such problems as vaccine therapy, inoculation against pneumonia, therapeutic immunization, methods of study of tuberculosis, vaccine therapy and immunity. The last paper published in 1942 is entitled 'On the need for abandoning much in immunology that has been regarded as assured'. In addition there are four appendices.

THE SICK AFRICAN: A CLINICAL STUDY.—By Michael Gelfand, M.B., Ch.B., M.R.C.P. (Lond.). The Stewart Printing Co. (Pty.) Ltd., Cape Town. Pp. 373. Price, 25s.

THE general idea of this book appears to us to be an excellent one, the description, mainly clinical, of the diseases prevalent among the Africans. The two first and the longest chapters are on the patient and on the examination. These chapters are excellent. Then follow 32 other chapters covering the diseases commonly found in Africa. These chapters average about 10 pages in length and here lies the great difficulty, that of discussing such a large variety of diseases, etiology, symptomatology, pathology, diagnosis, treatment and prevention, in such a short space. In so far as space had allowed, this has been well done, but of course such condensed presentation of the individual diseases must have big limitations. The book is intended not only for medical practitioners but for sisters, missionaries and African medical assistants. It is a great help to anyone working in a particular

country to have a book describing the diseases of that country. The same idea might be applied to other countries, but such books would not replace the larger, more exhaustive works.

ENDOCRINE MAN: A STUDY IN THE SURGERY OF SEX.—By L. R. Broster, O.B.E., D.M., M.Ch. (Oxon.), F.R.C.S. (Hon.), F.A.S.A. 1944. William Heinemann Medical Books Ltd., London. Pp. xl plus 144. Price, 12s. 6d.

THIS book is a most interesting and stimulating study, and covers a wider sphere than is indicated by its title or sub-title. It starts with a discussion of cell evolution in relation to instinct, and then discusses instincts of growth, self-preservation and reproduction and the way in which the expression of these instincts is influenced by the pituitary, adrenals and gonads. Side by side with the endocrine system has been evolved the central and autonomic nervous systems, and there is postulated a close association and co-operation between nervous and endocrine control which markedly influences structure, function and behaviour. Heredity and evolution are discussed, and the evolution of the nervous system and of the endocrine system. A chapter is devoted to the adreno-genital syndrome, and finally two chapters are devoted to symbiosis and parasitism, and the nature of man. The book ends as follows:—

'Such a theory therefore envisages the intermediate but vital rôle played by the endocrine system in the integration of development as a whole, and suggests that variable factors may be introduced into the germ plasma through its hormones to account for influences, which, on the whole, have consistently led to the progress of mankind.'

J. L.

Abstracts from Reports

THE SOUTH AFRICAN INSTITUTE FOR MEDICAL RESEARCH; ANNUAL REPORT FOR THE YEAR ENDED 31ST DECEMBER, 1943. JOHANNESBURG

THE work of the South African Medical Corps Establishment is under the Director of the Institute. This consisted in administration of the laboratory service, giving training in tropical medicine, laboratory techniques and blood transfusion, organizing transfusion service, etc. Protective vaccines and curative sera were prepared in vast amounts to meet military demands. Research work, in addition to investigations of military significance, was continued in the various departments. Steady progress has been made in the enzyme purification and concentration, of antitoxin; the work has made it possible to plan for the large scale production of antitoxins. Experiments were carried on the prophylaxis of typhoid fever by the intradermal injection of typhoid vaccine. The results proved satisfactory, its advantage being in the smaller quantity of vaccine required and also the elimination of general and local reactions. Work is proceeding to determine whether it is practicable to employ alum-precipitated vaccine satisfactorily using one injection only. Such a 'one shot' vaccine would be particularly valuable where the difficulty of recalling persons for a second injection is considerable. An outbreak of typhus in the Transkei territory was investigated, and it was proved for the first time that the epidemic was transmitted by lice. Serological tests for the diagnosis of typhus were also investigated and it was found possible by means of these tests, using pure rickettsial suspensions as antigens, to differentiate clearly between epidemic typhus, murine typhus and tick typhus. Other researches included identification of insects of medical importance, flea surveys, study of nutrition problems, etc. In addition

the institute carried out considerable routine diagnostic work. The serum department was expanded to meet war demands. During the year 2,040 litres of serum were prepared for transfusion services, and a large scale serum drying plant was completed. Also very large quantities of stock and autogenous vaccine were produced to meet the growing demands, including typhus vaccine of which nearly 40,000 doses were being prepared each month.

45TH ANNUAL REPORT OF THE INCORPORATED LIVERPOOL SCHOOL OF TROPICAL MEDICINE, 1943-44

AFTER recording deaths and changes in the staff, the report states that short courses of tropical medicine and parasitology for medical officers of the services were continued until December 1943. During the year under review five such courses were held with an attendance of 182 officers. Moreover, a number of officers attended the school to see the work and get what instruction could be given them in the course of the daily routine. Arrangements were made whereby the duties within the department of tropical medicine in future are broadly to be subdivided into (a) research, (b) teaching, and (c) clinical out-patient and hospital work and consultation practice. War conditions have enormously increased the incidence of tropical diseases in Europeans particularly those in the services. Some 1,400 in-patient cases were treated, and there were more than 2,000 out-patient attendances at the school. In addition, about 20,000 specimens for clinical pathological examinations were dealt with. A very considerable amount of time and effort were devoted to investigation of the treatment of malaria, in conjunction with Imperial Chemical Industries Ltd.; sundry new compounds were treated for their value as antimalarial therapeutic agents. The work shows much promise. At the invitation of the Colonial Office, Professor Blacklock visited West Africa to report on progress there in the prevention of mosquito-borne diseases, especially malaria. He is also serving in a Colonial Office Committee, the object being to inaugurate a scheme of research with a view to the development of suitable and safe types of houses for the indigenous people. Professor Davey at the request of the War Office, devoted a great part of his time during the year to the preparation of new specifications for substitute mosquito- and sandfly-netting; these specifications have now been adopted by the army. The work on scabies, which is being carried out for the War Office, is nearing completion, and a number of papers have been published. Various methods of breeding and infecting with malaria sterile mosquitoes are being investigated, with the object of studying the early stages of development of the malaria parasites in tissue culture. A new department of chemotherapy has been created in order to continue the researches on chemotherapy carried out under the Late Professor Warrington Yorke and here some interesting investigations are proceeding.

THE MISSION TO LEPERS

A REPORT OF THE SEVENTIETH YEAR'S WORK IN INDIA AND BURMA. SEPTEMBER 1943 TO AUGUST 1944

THIS report maintains its usual attractive form. The mission maintains institutions with nearly 7,000 patients in different parts of India and also gives aid to other institutions with 2,700 patients.

This report records the tragic death of Dr. G. B. Archer, M.D., at the home at Purulia. His work is being carried on by Dr. A. T. Roy. Another sad loss by death is that of Rai Sahib Dr. S. M. Ghosh, medical superintendent of the Leper Home, Raniganj. The report also records the death of Dr. Sudarsana Rao of Salur.

The report gives details of the work done in the homes of the mission and in the aided homes in Assam, Bengal, Bihar, Bombay, Central Provinces, Berrar, Madras, Orissa, Punjab, United Provinces, and Indian States. The report is illustrated with excellent

photographs illustrating the medical, religious, educational, agricultural, and other activities of these homes. In addition to treatment of the in-patients, over 9,000 out-patients are also treated.

In these pages we have frequently referred to the great quantity and the fine quality of the work done by this institution for those suffering from leprosy in this country. The budget for the work in India for the year 1943 was over 11½ lacs of rupees.

Correspondence

CEREBRAL MALARIA

Sm,—I have read Colonel Viswanathan's paper on 'Cerebral malaria' (*I.M.G.*, October 1944, p. 455) with much interest. With reference to his statement on page 456, lines 33-35 that '... the red cells containing the subtertian parasites are smaller in size than normal ...', I would like to point out that the corpuscles parasitized by large ring forms of *Plasmodium*

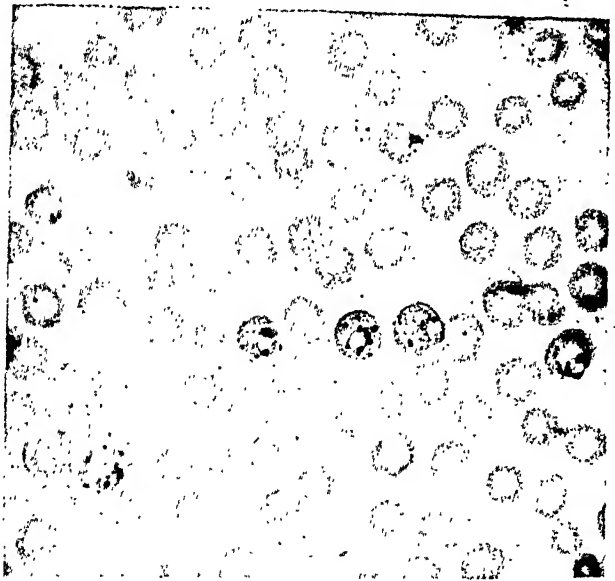


Figure showing blood smear from a case of *P. falciparum* infection. Photomicrograph (X 900 approx.).

falciparum are, however, often somewhat enlarged but never reduced in size as will be seen from the photomicrograph of a blood film showing *P. falciparum* infection.

B. M. DAS GUPTA.

CALCUTTA,
16th February, 1945.

QUININE SULPHATE FOR INTRAMUSCULAR INJECTIONS

SIR,—Christie McGuire and others described in the December 1943 issue of the *Indian Medical Gazette* a method for preparing a solution from quinine sulphate for intramuscular use. I have not got this particular issue, but I am sure that they did not give any reference from the past. They seem to think (or at any rate convey the impression to the reader) that this is entirely a new method evolved by them. It is nothing of the kind.

Only this afternoon, I was reading 'Tropical Diseases' (1903) by Sir Patrick Manson. He writes on page 158, 'if neither of these salts (*viz.* quinine, acid hydrochloride and hydrobromide) can be procured, the sulphate may be used, solution being effected by adding half its weight of tartaric acid'.

Further on we read, 'Benson, speaking from an experience of 1,390 cases, says that the hypodermic injection of quinine is by far the most effectual, as well as the most economical way of treating malarial fevers. He used the sulphate dissolved in water with the aid of hydrochloric acid, the strength of the solution being fifteen grains to the drachm; of this he injected twenty minims between the scapula, or into the outer surface of the arm. In 614 consecutive cases so treated not a single untoward accident occurred, one injection usually sufficing'.

I do not know who Benson is (or was), nor does Sir Patrick give any reference.

K. A. SHAH.

RANCHHODIAL DISPENSARY,
AHMEDABAD,
11th November, 1944.

[While we publish this letter, we regret in many ways so much discussion in our pages of intramuscular injections of quinine which are very rarely needed and which are so much abused. We have recently treated one patient with a very serious necrosis and abscess of the gluteus maximus resulting from an intramuscular injection of quinine, and several such cases have recently been seen in Calcutta hospitals. The abuse of intramuscular injections of quinine seems to us to be on the increase and it cannot be too strongly condemned. Not one patient of malaria in a thousand needs intramuscular quinine.—EDITOR, I.M.G.]

Service Notes

APPOINTMENTS AND TRANSFERS

LIEUTENANT-GENERAL J. B. HANCE, C.I.E., O.B.E., K.H.S., is appointed Officer on Special Duty in the office of the Director-General, Indian Medical Service, with effect from the 2nd December, 1944.

The services of Major-General W. C. Paton, C.I.E., M.C., K.H.P., are placed at the disposal of the Government of Bengal, with effect from the 24th December, 1944.

The Viceroy and Governor-General has been pleased to make the following appointment on His Excellency's Personal Staff:—

To be Honorary Surgeon

Colonel N. Briggs. Dated 17th July, 1944, *vice* Major-General J. P. Huban, O.B.E., vacated.

Lieutenant-Colonel P. A. Dargan, I.M.S. (Retd.), is appointed to officiate as Chief Medical Officer and Civil Surgeon, Delhi, with effect from the afternoon of the 30th November, 1944, *vice* Lieutenant-Colonel R. McRobert, whose services are replaced at the disposal of the Government of Burma from that date.

Major Jaswant Singh, Assistant Director, Malaria Institute of India, is appointed Deputy Director of the Institute, with effect from the 1st September, 1944.

The probationary appointments of the under-mentioned officers are confirmed with effect from the dates specified:—

27th September, 1939

Captain W. M. McCutcheon.
Captain G. S. Michelson.
Captain J. Aitken.
Captain P. W. Kent.
Captain R. O. Yerbury.
Captain P. J. Wormald.
Captain G. T. M. Hayes.
Captain J. P. O'Riordan.
Captain H. Rees.
Captain D. S. Wilson.

12th May, 1939

Captain D. F. Eastcott. Captain L. H. Cooper.
Captain A. M. McGavin. Dated 15th May, 1937.

Captain A. S. Brown. Dated 19th October, 1939.
INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

To be Captains

Sukomal Sen. Dated 6th July, 1943.
Pradyumna Narayan Singh Jayaswal. Dated 17th September, 1944.
Digambar Narayan Mazumdar. Dated 20th September, 1944.
Sudhir Kumar Saha. Dated 20th September, 1944.
Vengangudi Srinivasa Annaswamy. Dated 19th October, 1944.
Audisheshaiah Marella. Dated 20th October, 1944.

5th February, 1944

Pirthvi Nath Kanwar. Ghulam Mohd.
Hafiz-Ur-Rahman. Ghulam Nabi.

14th November, 1944

Bhagwandas Wadhmal Jogendra Lal Basak.
Advani. Subodh Chandra Kar.
Krishna Rao Purohit. Dated 19th October, 1944.
Angara Satyagnana Rao. Dated 24th November, 1944.

To be Lieutenants

14th November, 1944

Mushtaq Ahmad Chaudhri. Sahibzada Rashid-Ul-
Mushtaq Ahmad. Hamid.

Rashid Ahmed Khan.

Mohd. Sadiq Khan. Dated 15th November, 1944.
Iqbal Singh Dhingra. Dated 16th November, 1944.

19th November, 1944

Kanwar Sain Isar. Asghar Nizami.
Ahmad Din Salah-Ud-Din. Jai Krishan Sehgal.
Mahendar Pal Bhalla. Khalil Ahmad Malik.
Mohammad Anwar Choudhrie. Dated 18th November, 1944.

21st November, 1944

Bhagat Chand Bhoil.
S. Mohammad Hasanain Bokhari.

INDIAN MEDICAL SERVICE

(Emergency Commissions)

To be Lieutenants

A. B. Philip. Dated 6th November, 1943.
6th October, 1944

Mervyn David Sopher. Asoke Kumar Mitra.
Dinendra Narayan Bhowmik.
Anil Baran Ray. Dated 14th October, 1944.
Adhir Kumar Ganguly. Dated 20th October, 1944.
Bhupendra Kumar Bardhan. Dated 24th October, 1944.
Perumaulpeta Dorai Raj. Dated 19th November, 1944.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
(Emergency Commission)

To be Lieutenant (on probation)

Krishna Gopal Kapoor. Dated 15th March, 1942.

INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

(WOMEN'S BRANCH)

To be Lieutenants

(Miss) Soona Jamshedji Mistry. Dated 3rd November, 1944.
(Miss) Una Hargreaves. Dated 11th November, 1944.

PROMOTIONS

Colonel (Temp. Major-General) Sir John Taylor, C.I.E., D.S.O., is granted the honorary rank of Major-General on reversion to Retired List. Dated 14th February, 1944.

Colonel to be Major-General

G. Covell, C.I.E., K.H.P. Dated 17th July, 1944.

Lieutenant-Colonels to be Colonels

W. E. R. Dimond, C.I.E., O.B.E. Dated 15th April, 1944.

D. Clyde, C.I.E. Dated 17th July, 1944.

D. V. O'Malley, O.B.E. Dated 30th July, 1944.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS*(Emergency Commissions)**Captains to be Majors*

E. J. Ramdas. Dated 2nd December, 1944.

S. F. Seelig. Dated 8th December, 1944.

B. C. Roy. Dated 14th December, 1944.

B. K. Sheorey. Dated 23rd December, 1944.

Lieutenants to be Captains

V. N. Vadhwakar. Dated 4th December, 1944.

F. Hasan. Dated 5th December, 1944.

J. Narain. Dated 7th December, 1944.

J. Harinarain. Dated 8th December, 1944.

20th December, 1944

M. D. Murphy. B. P. Singh.

T. C. Prabhakar. Dated 27th December, 1944.

K. J. Verghese. Dated 28th December, 1944.

K. R. Venkatachalapathy. Dated 16th November, 1943.

B. P. Reddy. Dated 28th December, 1943.

D. I. Gantzer. Dated 21st July, 1944.

3rd November, 1944

G. S. Sekhon. M. Singh.

S. N. Sahibzada. B. S. Sidhu.

S. L. Khosla. K. S. Hasan.

A. A. Awan. B. A. Bhatti.

K. D. K. Sherwani. A. M. Yusuf.

O. Jacob. J. Singh.

G. S. Sarin. G. D. Kapur.

L. D. Sachdeva. M. Hasan.

M. Z. Abid.

D. H. Waller. Dated 4th November, 1944.

6th November, 1944

T. M. Niaz. M. Ghiaz-Ud-Din.

B. Ahmad. Dated 8th November, 1944.

14th November, 1944

C. S. Narain. K. J. Raju.

15th November, 1944

M. M. Chauhan. D. K. Murthy.

A. Venkatachalam. T. Joshua.

17th November, 1944

S. N. Venkataraman. G. V. L. D'Sena.

A. Shivabooshanam. M. D. Innis.

H. A. Garstin. Dated 21st November, 1944.

J. Yates. Dated 24th November, 1944.

29th November, 1944

M. M. Ali. P. R. Govind.

30th November, 1944

M. C. Gupta. S. K. Kochhar.

(Miss) K. N. Chand Lai. Dated 2nd November, 1944.

A. G. Sheikh. Dated 5th November, 1944.

SECONDED FOR SERVICE WITH THE ROYAL INDIAN NAVY

*(Emergency Commissions)**Lieutenants to be Captains*

Satya Prakash. Dated 4th November, 1944.

C. M. Chandrasekaran. Dated 17th November, 1944.

Dev Nath. Dated 21st November, 1944.

A. V. Bal. Dated 16th December, 1944.

SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(WOMEN'S BRANCH)*Lieutenants to be Captains*

(Miss) L. B. Bhawe. Dated 20th December, 1944.

(Miss) M. E. Lazarus. Dated 21st December, 1944.

RETIREMENTS

Lieutenant-Colonel T. S. Shastri. Dated 22nd October, 1944.

Major W. G. Kingston, on account of ill health. Dated 27th December, 1943.

RESIGNATION

The undermentioned officers are permitted to resign their commissions and are granted the honorary rank of Captain subject to His Majesty's approval:—

INDIAN MEDICAL SERVICE

SECONDED TO INDIAN ARMY MEDICAL CORPS

*(Emergency Commissions)*Captain (Mrs.) B. F. Dickinson (*nee* Thomas). Dated 20th July, 1944.Captain (Mrs.) L. M. Corall (*nee* James). Dated 2nd November, 1944.

RELINQUISHMENTS

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE

SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commission)

Captain Bashir Ahmad Bhatti. Dated 5th November, 1944, on grounds of ill health and is granted the honorary rank of Captain.

INDIAN MEDICAL SERVICE

(Emergency Commission)

Captain H. M. Garlick relinquishes her commission on account of ill health and is granted the honorary rank of Captain. Dated 6th January, 1944.

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Original Articles

OCULAR COMPLICATIONS IN
SMALLPOX*

By CAPTAIN K. SEN, M.B., D.O.M.S., F.R.C.S.E.

Honorary Ophthalmic Surgeon, Medical College Hospitals; Late Honorary Teacher in Ophthalmic Surgery; Honorary Ophthalmic Surgeon, Campbell Medical School and Hospitals, Calcutta

It is admitted that smallpox is one of the commonest causes of blindness in India, and specially so in Bengal, where the disease is endemic, and epidemics are of frequent occurrence every 3 or 5 years. In foreign literature, the following complications are mentioned: catarrhal conjunctivitis, conjunctival and corneal pustules, corneal ulcers, hypopyon ulcers causing dense leucomata, and vitiligo of the iris. 'Hypopyon ulcers of smallpox used to be of importance because of its prevalence in pre-vaccination days: it used to account for 35 per cent of all blindness, but now it is rare except in countries where smallpox is rife and nursing is poor' (Duke-Elder, 1937). No Indian records are available giving details of the cause of blindness in smallpox.

The study was undertaken in the Campbell Hospital during the period 1932-1939 with a view to finding out the causes of blindness in smallpox and the prevention of blindness, if possible. The study is divided into 4 parts:—

(1) Observations of pathological conditions of the eyes already blind due to smallpox amongst the outdoor cases, 1932-1935.

(2) Observations on cases of smallpox after they had developed ocular complications, 1933-1935.

(3) Observations on all cases of smallpox admitted into the hospital during the epidemic of 1936 (January to May).

These observations form the basis of this paper.

(4) Observations on all cases admitted into the hospital up to the epidemic of 1939 with special reference to the preventive measures adopted against blindness.

(1) Observations amongst outdoor cases,
1932-1935

Forty-three cases of blindness due to smallpox were observed. The blindness was due to (a) phthisis bulbi—9 cases, two were bilateral, and seven unilateral, (b) dense leucoma involving the whole of cornea—14 cases, three

were bilateral, and eleven unilateral, (c) dense leucoma with secondary glaucoma—6 cases, four unilateral and two bilateral, (d) leucoma with anterior synechia—6 cases, two bilateral, and four unilateral. All patients in the last group had some sight after separation of the anterior synechia and optical iridectomy. All these cases point towards corneal complications, primary or secondary.

(2) Observations amongst indoor cases,
1933-1935

During this period, methylene blue drops (1 per cent) were used as routine in all cases, and liquid paraffin drops in all unconscious or semi-conscious cases twice daily. The services of the ophthalmic surgeon were requisitioned after the development of some serious complications. It was striking to see large number of cases of muco-purulent conjunctivitis, corneal ulcer, hypopyon ulcer, and lagophthalmic keratitis. Many patients left the hospital cured of smallpox but blind in one or both eyes. It was observed that ocular complications were more common in the epidemic year of 1933 than in the endemic years of 1934 and 1935. The discharge from some cases of muco-purulent conjunctivitis were examined. On culture, the most common organisms found were *Staphylococcus albus*, *citreus* or *aureus*, Koch-Week's bacilli, diphtheroid bacilli, and very occasional streptococci and pneumococci. In every case of hypopyon ulcer where the lacrimal sac could be examined, there was regurgitation from the sac, but this examination was not possible in the majority of cases due to the eruption and swelling of the part. It was clear that the clue to the prevention of blindness was in the prevention of corneal ulcers.

At the end of 1935, preventive measures were adopted. For this purpose two trays were introduced. The surgeon's tray contained two Desmarre's lid elevators, two canaliculus dilators, and a small glass-stoppered phial of pure carbolic acid. The nurse's tray contained one large undine containing 1 in 15,000 oxycyanide of mercury lotion, one large pot of sterile boracic ointment, argyrol drops 4 per cent and 10 per cent, and two glass rods to introduce the ointment. Oxycyanide of mercury lotion was selected to wash out the eyes as it was supposed to have some specific action against staphylococci. The following routine method was introduced:—

(a) On admission, the lacrimal sac was examined whenever possible. In all cases of diseased and doubtful lacrimal sacs, the puncta lacrimalis and parts of canaliculi were cauterized by the surgeon with pure carbolic acid by means of a canaliculus dilator.

(b) In all cases with conjunctival discharge, the eyes were washed out 3 times daily with the lotion from an undine and more frequently in serious cases as desired by the surgeon.

*[Paper condensed by editor. This work was done in the period before sulphonamides became available; these drugs may have markedly changed the situation.—Editor, I.M.G.]

(c) The routine use of either 4 per cent or 10 per cent argyrol drops according to the severity of the case in all cases of conjunctivitis was instituted.

(d) In every case of conjunctivitis, boric ointment was introduced twice daily morning and night so that the lids might not stick together.

It should be noted that this routine treatment aimed at isolating the infected lacrimal sacs, prevention and treatment of acute conjunctivitis, and the prevention of lagophthalmic keratitis.

(3) *Study of all cases of smallpox admitted into the hospital during the epidemic of 1936*

All observations in this paper were from the records of the cases during the months from January to May (see tables I and II). The preventive and curative work was done under the direct supervision of the ophthalmic surgeon. All cases are included except those who were admitted during afternoon and night and expired before the next morning. During the period, 1,929 cases were admitted, of which 236 had ocular complications; 185 cases were admitted with these, and

cases show growths of *Staphylococci albus* or *aureus* or a mixed growth' (Sen, 1935).

The more severe the disease the more are the ocular complications. The hæmorrhagic type is the most severe, but most of the patients died so quickly that they could not be examined for ocular complications. 4.7 per cent amongst those who were examined was a high figure considering the short period between the attack and death.

(4) *Ocular complications as observed in 236 cases*

In 185 of these, the complications were present before admission to hospital. In 51, however, the complications developed after admission. Of these, 19 showed smallpox vesicles and pustules, 5 showed phlyctenular keratitis and 7 showed sub-conjunctival hæmorrhages attributable to smallpox. In 20 of the 51 cases, the eye lesions were caused either by secondary infection or by keratomalacia and were therefore preventable. At the time this work was done however sulphonamides were not available.

The nature of the ocular complications of smallpox encountered in these 236 cases is in-

TABLE I
Incidence by month

	January	February	March	April	May	Total
Admissions ..	250	509	678	397	93	1,929
Ocular complications ..	21	39	118	49	9	236
PERCENTAGE ..	8.4	7.6	17.4	12.3	9.6	12.2

51 developed ocular complications in the hospital in spite of the preventive measures.

The worst months of the epidemic were February and March, but the worst months for the ocular complications were March and April. The epidemics of 1933 and 1939 showed a similar phenomenon. Probably this is due to an increase in the conjunctival infection from the end of February. It was observed that at the end of the winter, when the days are warming up from the end of February, conjunctival sacs without any growth become fewer and more

indicated in table III. The complications are divided into two groups, one caused by smallpox and the second caused by complications. It will be seen that the latter group is much larger. Vesicle and pustule formation on the conjunctiva, sclera and cornea, and sub-conjunctival hæmorrhage constitute group I caused by smallpox and they together are responsible for 19.7 per cent of the ocular complications. Inflammatory conditions of the conjunctiva and cornea with secondary infection and cases of keratomalacia constitute 79.3 per cent of cases.

TABLE II
Ocular complications according to type of the disease

Types of smallpox	Confluent	Semi-confluent	Discrete	Hæmorrhagic	Discrete
Admissions ..	1,083	319	191	127	209
Ocular complications ..	195	26	5	6	4
PERCENTAGE ..	18.3	8.1	2.6	4.7	1.9

TABLE III
Ocular complications of smallpox

	Total number of cases	Percentage
Group I		
Conjunctival vesicles and pustules.	20	8.4
Corneal vesicles and pustules.	7	2.5
Sclero-corneal vesicles and pustules.	12	5.0
Sub-conjunctival hæmorrhage.	9	3.8
		19.7
Group II		
Acute conjunctivitis ..	27	11.4
Muco-purulent conjunctivitis.	97	41.1
Muco-purulent conjunctivitis with corneal ulcer.	20	8.4
Phlyctenular keratitis ..	10	4.2
Lagophthalmic keratitis (exposure keratitis).	23	11.8
Perforation of cornea, iris prolapse.	3	1.2
Acute keratomalacia ..	3	1.2
		79.3
	236	99.0

The vesicles and pustules of the conjunctiva, sclera or cornea developed during the stage of skin eruptions, the conjunctival lesions being usually bilateral but the sclero-corneal lesions being mostly unilateral. On the conjunctiva, they were found on the exposed part of the bulbar conjunctiva of the palpebral fissure or on the caruncle. The vesicle appeared as small raised areas with mild local reactions and on bursting left no trace. The pustules which were more numerous, caused severe reaction and pain, and soon the area was covered with a slough after the separation of which the healing was fairly rapid. The lesions of the cornea were similar. When they healed they were followed by a dense leucoma but the whole cornea was not affected and some sight was left.

Inflammatory complications varied from simple conjunctivitis to the severer forms of conjunctivitis, keratitis, hypopyon ulcer and perforation of the cornea with prolapse of the iris. The largest group of cases was muco-purulent conjunctivitis. This usually cleared up and left no blindness but, in some, complications were seen such as marginal ulcer. The corneal complications however, though less numerous, were much more serious. Forty-four cases showed serious affection of the cornea, and the rapid development in some of the cases was very remarkable. Within 24 hours of the development of multi-corneal ulcer the cornea became quite opaque and within the next 24 hours it was completely blurred. In these patients deaths were numerous. It was later

believed that these were really cases of acute keratomalacia but they have not been entered as such in the table.

Some other conditions were seen such as exposure keratitis, perforation of the cornea with iris prolapse, but not a single case of hypopyon ulcer was seen, which is strange considering the fact that it had previously been reported as common in smallpox in Calcutta.

Summary.—An account is given of the ocular complications of smallpox seen in Calcutta during the years 1932 to 1939. The analysis shows that only a minority of the complications were caused direct by smallpox and that in the causation of these complications and of the blindness which frequently follows, secondary infection and acute keratomalacia play an important part. It is believed that these complications could now be prevented or controlled by the routine administration, in cases of smallpox, of the sulphonamides and vitamin A.

The writer was very grateful to Lieut.-Colonel N. C. Kapur, I.M.S., the Superintendent of the Campbell Hospital in 1935 in allowing him to introduce the preventive measures, examine and treat all the cases in the smallpox ward. His thanks are also due to Dr. H. N. Bakshi and Dr. B. C. Chatterji, medical officers in charge of the ward for their help and co-operation, and Dr. B. N. Banerji for collecting the statistics of all cases with ocular complications and to Dr. A. Majumdar for collecting the statistics of all cases admitted into the hospital.

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FRACTURE-DISLOCATION OF THE CERVICAL SPINE

A CASE REPORT

By N. S. MACPHERSON, F.R.C.S.

Surgeon

and

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A CASE of fracture-dislocation of the cervical spine occurred recently in the practice of the Medical College Hospital, Vellore, in which post-mortem examination five days after the accident gave the opportunity to determine the exact nature of the injury and of the mechanism of both displacement and reduction.

Clinical report.—The patient was a Hindu male aged 52. Two days before admission, he was carrying a heavy load on his head; finding it too heavy, he shifted it from his head and in so doing fell down. From that time he was unable to move either arms or legs or to feel anything below the level of his shoulders. It was not possible to find out the exact mechanical cause of the injury beyond the fact that it

involved the sudden alteration in the position of a heavy weight carried on the head.

On admission to hospital on 10th September, 1944, his temperature was subnormal, 97°F ., his pulse rate very slow, 43, respiration rate 28, but after 8 hours the temperature had risen to 98.4°F ., and pulse rate to 53. Twenty hours after admission the temperature was 100°F ., pulse rate 66, respiration rate 26. His general condition did not cause immediate anxiety, and he was not distressed in any way.

He complained of slight pain in the back of his neck but said that he could neither feel nor move any part of his body below the level of the clavicles. Complete flaccid paralysis of and complete loss of sensation over the trunk and all the four limbs were present. The upper level of the sensory disturbance was only approximately determined. There was no respiratory embarrassment. The bladder was much distended and faeces had been passed involuntarily. There was no obvious distortion of the neck, and the head was not turned to either side but occupied an apparently normal position; there was tenderness on palpation posteriorly over the mid-cervical vertebrae.

Radiologist's report

'X-ray of the cervical and upper dorsal spine shows a dislocation of the 4th cervical vertebra forward on the 5th cervical vertebra, the displacement being about equal to half the width of the vertebral body. The 4th cervical is tilted slightly downward over the 5th cervical. In the antero-posterior view the inter-vertebral space between C. 4 and C. 5 appears narrowed, that between C. 5 and C. 6 appears slightly wider than normal. No fracture is demonstrated' (figures 1 and 2).

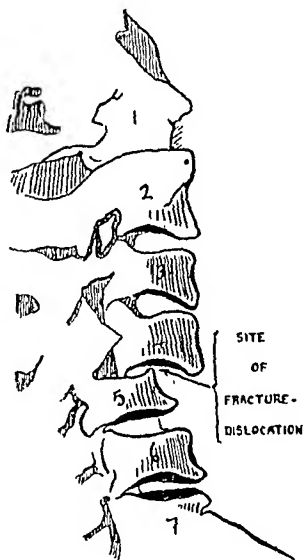


Fig. 1.—Lateral view. Before reduction.

In the afternoon of 11th September, 1944, the patient was anaesthetized with chloroform and ether mixture and an attempt made to reduce the dislocation by traction with the neck hyperextended, but beyond widening of the space between the bodies of the involved vertebrae no effect was produced (figure 3). Then gentle

rotation of the neck with lateral abduction was tried and a slight but definite click-like sensation was felt though it was not possible to feel

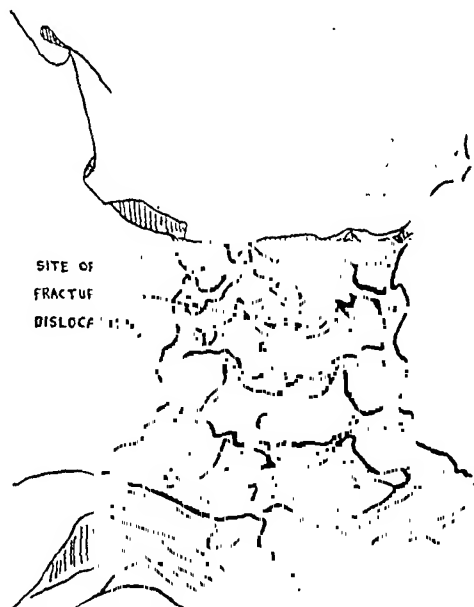


Fig. 2.—Antero-posterior view. Before reduction.

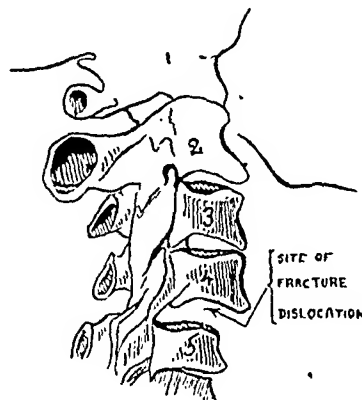


Fig. 3.—Lateral view. After first attempt at reduction.

or see any change in position. Further x-ray examination however showed that reduction had taken place (figure 4). The neck was then fixed

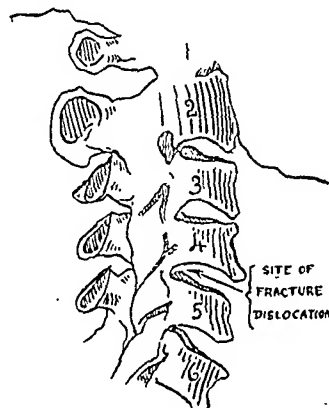


Fig. 4.—Lateral view. After reduction.

in a plaster splint around the head, neck and axillae.

On the next day, 12th September, 1944, the man's general condition was satisfactory and he had some sensation in his arms (T. 100.6°F., P. 76, R. 26); by the evening he was able to feel more in his arms and he also complained of pain in his legs: catheterization however was still necessary for retention of urine.

At 5 a.m. on 13th September, 1944, he suddenly developed difficulty in breathing, the respiration rate rose to 36, and there was fine froth in his nose and throat. Death took place at 9 a.m., and the appearance was that of acute pulmonary oedema.

Description of the specimen

Permission was not obtained for a general post mortem except for examination of the injured part, accordingly the cervical vertebrae from the 2nd to the 7th were removed.

Figure 5 shows the condition as seen from behind with the muscles removed for clarity. The cervical vertebrae from the 2nd to the 7th are present; between the 4th and the 5th

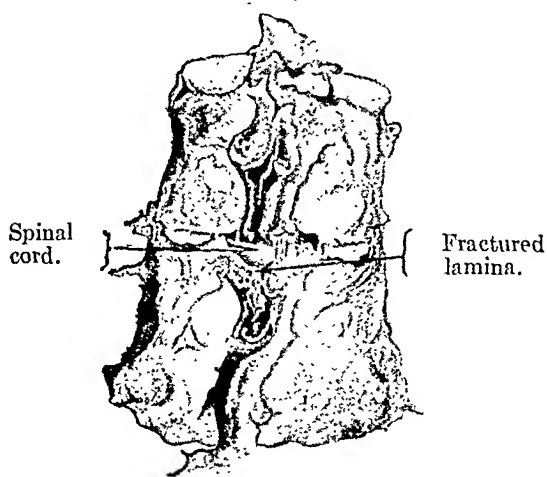


Fig. 5.—Posterior aspect as found at post mortem.

vertebrae the ligamentum nuchae and the ligamentum subflavum have been torn through, and the laminae fractured near the base of the spine of the 5th vertebra. Small pieces of bone are found in this situation, where the dura mater is exposed. Laterally, the joints between the articular processes of the two vertebrae have been torn open but the dislocation has been completely reduced and there is no pressure on the cord. The dura mater was opened and the cord inspected; there was no evidence of compression or bruising. The anterior aspect is shown in figure 6. The anterior longitudinal ligament is completely torn through opposite the body of the 5th vertebra and on lifting this torn ligament a small portion of the upper and anterior part of the body of the vertebra is found to be adherent to it.

It was comparatively easy to reproduce the dislocation as shown in figure 7. From behind, the articular processes of the 4th cervical vertebra are seen to have slipped in front of the superior articular processes of the 5th,

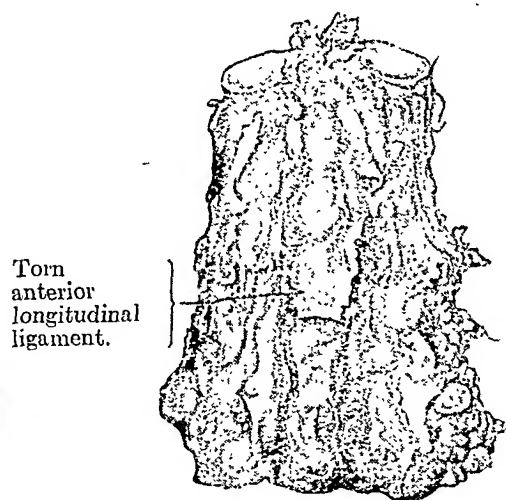


Fig. 6.—Anterior aspect.

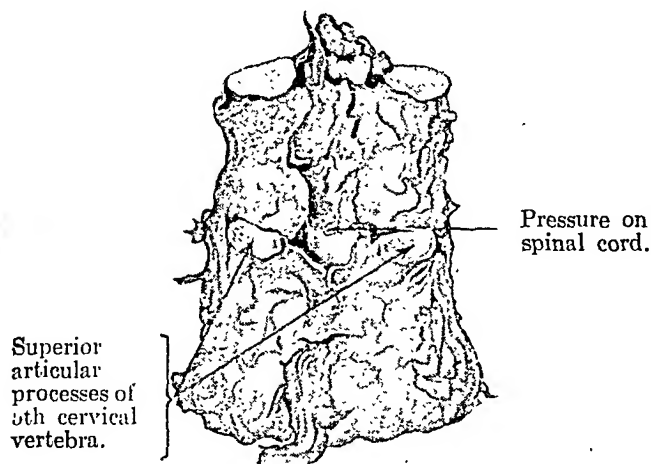


Fig. 7.—Posterior aspect. Dislocation reproduced.

causing well-marked pressure on the cord by the vertebral arch of the 4th. Attempts to reduce the dislocation by simple traction in extension were unsuccessful, but when abduction and rotation were used, it was most interesting to observe the way in which it could be reduced with ease, first on one side and then on the other.

Discussion

It is interesting to realize that as long ago as the third century B.C. such accidents were carefully observed. In his article on the Edwin Smith Papyrus in the *British Journal of Surgery* (1934), Power quotes three extracts in which the writer distinguishes between dislocation, cervical sprain and fracture-dislocation of

the cervical vertebrae. Concerning the latter two conditions he says :—

'Instructions concerning a displacement in a vertebra in his neck. If thou examinest a man having a displacement in a vertebra of his neck, whose face is fixed, whose neck cannot turn for him, and thou shouldest say to him "Look at thy breast and thy two shoulders" and he is unable to turn his face so that he may look at his breast and his two shoulders thou shouldest say concerning him "One having a displacement in a vertebra of his neck. An ailment which I will treat".'

and again :—

'Instruction concerning a crushed vertebra in the neck. If thou examinest a man having a crushed vertebra in his neck and thou findest that one vertebra has fallen into the next, while he is voiceless and cannot speak; his head, falling downwards, has caused that one vertebra crush into the next; and shouldest thou find that he is unconscious of his two arms and his two legs because of it thou shouldest say concerning him "One having a crushed vertebra in his neck; is unconscious of his two arms and his two legs and he is speechless. An ailment not to be treated".'

In his book on the 'Treatment of Fractures' Böhler (1935) gives illustrations of a condition almost identical with that described in this report except that it involves the 6th and 7th vertebrae. Dealing with the cause of such fractures he says : 'If the head and with it the neck are bent forward to an excessive degree there usually occur injuries of the middle and lower vertebrae.' In the case reported, it would appear likely that in trying to remove his load the man bent his head and neck forward and at this moment the load fell back on his vertex thereby causing the injury. That such an injury can occur with a sudden jerk apart from great violence is shown by the following statement by Watson-Jones (1943): 'I have seen two cases arise from an involuntary jerk of the head sustained by a passenger in a car which stopped suddenly and unexpectedly.' This emphasizes the paramount importance, for preserving the stability of joints, of the tone of the muscles surrounding them.

For treatment, both these authorities recommend immediate reduction of the dislocation by traction, Böhler using a Glisson's sling while Watson-Jones prefers skeletal traction by skull calipers. In the case described, neither of these appliances was available: had either of them been used it is possible that traction alone would have sufficed to reduce the deformity. Reference to an older textbook by Choyce and Beattie (1923) shows that the difficulty of reduction by manual traction was realized and the use of abduction and rotation advised. Experience with this patient may be of help and encouragement to those who may have to deal with such a condition away from the facilities of an up-to-date fracture clinic.

Böhler commenting on the signs of nervous injury and the prognosis of such a case makes the following comment: 'If the cervical cord is not torn but only compressed, sensation often returns a few hours after reduction. Voluntary movement returns partially or completely

in a few days or weeks, if there has been no hæmorrhage into the substance of the cord.'

The two chief points of interest in the case described are :—

1. The method of reduction which was found to be effective.

2. The fact that fracture-dislocation of the cervical spine can occur without injury to the cord other than compression, and that relief of this compression can be followed by an almost immediate return of function even when the pressure has been present for three days.

We are indebted to Dr. Ida B. Scudder for the radiological examinations and to Mr. Guiry for his drawings and copies of the skiagrams; also to Dr. R. G. Cochrane, Principal of the Medical College, Vellore, for criticism and for permission to publish this report.

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HEPARIN IN PENICILLIN THERAPY*

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THE systemic administration of penicillin presents certain difficulties. In many cases where penicillin therapy is indicated, the patient is very ill, tired and weary; he may have had injections of morphia, anti-tetanic serum and anti-gas gangrene serum at intervals, not to mention blood or plasma transfusion and operative procedures. For these reasons, it is important that penicillin therapy should entail one prick after which the patient should have no more inconvenience. Intramuscular injections of penicillin are tedious and may be very painful to the patient. Intravenous injections at intervals are also a burden. An intramuscular drip may accomplish this, but in my experience unless the dose of penicillin is concentrated in a small bulk, i.e. 120,000 units in 500 c.cm. to be given over 24 hours, absorption is often not complete; moreover, even in more dilute solutions severe pain at the site of injection is generally experienced after 48 to 72 hours, and the injection has to be stopped and recommenced in another situation. The intravenous drip is comfortable to the patient, ensures the solution reaching the blood stream and tissue fluids, and in a few cases a full course of treatment can be completed; but we have found that thrombosis or thrombo-phlebitis generally occurs after a period varying between 18 hours and 5 days, usually between 24 and 72 hours and another vein has to be used.

* Paper rearranged by editor.

Batches of penicillin vary in their irritant properties, as also does the pain in continuous intramuscular injection, and it is reasonable to suppose that the irritant properties are due to the impurities in the preparation rather than to the penicillin itself. In a series of cases where the continuous intravenous drip method was used, the addition of heparin to the penicillin solution proved to be of undoubted value in preventing thrombosis or thrombo-phlebitis, enabling the full course of treatment to be completed via one vein without mishap, and without discomfort to the patient.

Heparin has been shown to be non-toxic by Howell and McDonald (1930), and by Murray (1940). Hedenius (1937) has shown that it causes no increase in coagulation time of the blood until a threshold of .25 mg. per kilo body weight is reached (and to reach this amount in an eight-stone man would require 14 mg. and in a ten-stone man between 17 and 18 mg.). As 15 mg. of heparin are destroyed hourly by the body, it would be necessary to give at least 15 mg. hourly in a man of 8 to 10 stones to cause any alteration in coagulation time. Now one Toronto unit contains .01 mg. of heparin, and thus 15 mg. would therefore represent 1,500 units. In the dosage of heparin suggested it will be seen that this amount will never be approached. It has been suggested that heparin might influence the potency of penicillin; this has been tested out by Green who found no evidence to support this contention.

In continuous intravenous penicillin therapy, a solution of penicillin in saline has been used, containing 30,000 units per 500 c.cm. to be given over six hours. To the solution we added at first 1 unit of heparin per c.cm., and this amount sufficed to allow a full course of penicillin to be given without untoward incident during the administration, although there was a tendency for the vein to thrombose after the needle was withdrawn. A later batch of penicillin was much more irritant; in fact, in one case, thrombosis occurred regularly after 24 hours' treatment on four occasions, and it was found necessary to add 3 units of heparin per c.cm. to the penicillin solution. Even so, in two cases treated with this batch, thrombosis occurred after three days, and the addition of 5 units

per c.cm. was found to be required to eliminate thrombosis completely. One case in this series is interesting and significant. After 20 hours the drip was in error stopped for 4 hours with the needle remaining *in situ*, without thrombosis occurring, and on restarting the drip, there was no interference with the rate of the flow.

A definite amount of heparin to be used cannot yet be laid down, but the dosage we employ is 3 units per c.cm. of penicillin solution, the heparin being added to the solution in the bottle. Should thrombosis occur with this, as it may occasionally, the next bottle is charged with 5 units per c.cm., when it is improbable that any further trouble will be experienced with the course of the drip infusion.

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MATERNAL BLOOD IN WHOOPING COUGH*

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HUMAN convalescent whooping cough serum and whole blood injected intramuscularly have been tried and reported on favourably in whooping cough cases as a curative and prophylactic measure. Some workers claim good results from treatment with injection of maternal whole blood. The writer tried this latter method of treatment in a series of 76 cases, out of which 3 discontinued treatment and one died a day after the commencement of treatment. This report embodies the observations on the remaining 72 cases including controls.

Most of the cases were treated as out-patients in 3 different hospitals. Some were treated at home in private practice. The early cases of this series came during the course of an epidemic, which was severe but limited and circumscribed.

Age and sex.—The age and sex distribution of the cases are shown in the following table:—

* Paper rearranged by editor.

TABLE I

Sex	AGE IN YEARS										Total
	Under 1 year	1-2	2-3	3-4	4-5	5-6	6-7	7-8	8-9	9-10	
Male	..	4	8	7	5	3	2	2	1	1	33
Female	..	5	8	9	7	5	3	1	39
TOTAL	..	1	9	16	16	12	8	5	3	1	72

Diagnosis.—The diagnosis was clinical and based in the majority of cases on the presence of typical whoops.

Out of 72 cases, 8 were seen in the catarrhal stage and the rest in the paroxysmal stage. In the catarrhal stage the diagnosis was based on the history of exposure to the infection or presence of the disease in other children of the family and cough assuming gradually to be paroxysmal, especially at night and sometimes culminating in vomiting.

Blood count was done in 11 cases, which showed leucocytosis (16,000 to 30,000 white cells per c.mm. of blood) with a relative lymphocytosis, varying from 46 to 72 per cent lymphocytes.

Method.—In the beginning every third case was taken as control, but subsequently as many of the cases as were possible were treated with maternal blood. Only 10 cases, mainly motherless children, were treated throughout as controls and treated with a mixture containing belladonna and bromides. Clinical examination of mothers was done to exclude constitutional

fitting from the treatment being thus 75.8 per cent. The rest did not benefit at all.

The duration of the disease before treatment varied from 5 to 6 weeks; no correlation was observed between the duration of the disease and response to treatment.

Only four mothers gave a history of suffering from paroxysmal cough, suggestive of whooping cough in their childhood, and 5 children were treated with their blood.

Children, whose mothers were pregnant, required a smaller number of injections, 4 to 5 injections being sufficient to effect a cure; in some cases 2 injections almost dramatically abolished the whoops. Altogether 14 children received blood from 10 pregnant mothers, and all of them were cured.

In the 10 control cases, the period for the disappearance of whoops varied from 2 to 10 weeks, whereas in cases receiving maternal blood it was 4 to 10 days.

The results, as observed in the first two weeks of treatment, have been tabulated below :—

TABLE II

Treatment with	Number of cases	CURED		IMPROVED		SLIGHT IMPROVEMENT		NO IMPROVEMENT	
		Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent
Mother's blood ..	62	41	66.1	6	9.7	15	24.2
Pregnant mother's blood ..	14	14	100.0
Non-pregnant mother's blood	48	27	56.25	6	12.5	15	31.25
Immune* mother's blood ..	5	3	60.0	1	20.0	1	20.0
Drugs (control cases) ..	10	3	30.0	4	40.0	3	30.0

* Immune mother means mother who had had whooping cough in her childhood.

and communicable diseases. Blood was taken from a vein with a syringe containing a little sterile citrate solution and injected immediately into the buttock. The dose varied from 5 to 15 c.cm. according to the age of the child, and the injections were given daily from 3 to 8 days. No other drug was administered during the course of injections except in 2 children who had broncho-pneumonia, for which sulphathiazole was given simultaneously. Disappearance of whoop and distressing cough was taken as the criterion of cure.

Results and observations.—Out of 62 cases treated with maternal blood, 41 (66.1 per cent) were cured in 4 to 10 days as judged from the disappearance of whoops; slight cough and catarrh persisted, for which adexolin or cod-liver oil and orange juice or *amla* (*Phyllanthus emblica*), and in a few cases ascorbic acid were administered along with the symptomatic treatment. With this the lingering catarrh disappeared in course of a fortnight, and the children improved much in health. In 6 cases (9.7 per cent) the frequency and intensity of paroxysms diminished, the total number bene-

Untoward effects.—No untoward effect was observed. In one case the mother was in incubation period of malaria and developed malarial fever after three injections were given to her child. On microscopical examination M.T. rings were found in her blood. Immediately the child, though afebrile, was also treated for malaria for five days. In spite of this, the child, a female, aged 6 years, three weeks after the last injection, developed a rather severe type of malaria showing M.T. rings in the blood but recovered with oral quinine. In this case, as the mother and child were living in the same house, it is possible that the latter might have been infected in the natural way by mosquitoes, but infection of the child through inoculation of infected maternal blood is also a possibility.

Discussion.—The benefit from the serum and whole blood of whooping cough convalescents is believed to be due to presence of specific immune bodies in the blood and serum of convalescents. In the series under report, four mothers gave history of suffering from suspected whooping cough in their childhood and

five children were treated with their blood. The result was not materially different from that of the other cases benefiting from maternal blood. It is also unlikely that their blood contained sufficient amount of immune bodies after lapse of so many years.

Moreover, pregnant mother's blood was found more potent. It would appear therefore that maternal blood contains something, which has the property of curing whooping cough when administered parenterally, and that this unknown substance is present in greater amount during pregnancy; conversely, the child's blood lacks this unknown substance.

The fact that whooping cough is predominantly a disease of childhood and only occasionally affects adults, points to the increased activity of the endocrines and readjustment of hormonal balance in the latter. These hormones are also present in greater amount and their production set at a higher level during pregnancy. Some of these hormones, either alone or in combination, might have the property of curing whooping cough.

The failure of treatment in some of the cases of this series might be due to hormonal imbalance in their mothers.

Summary.—Treatment of whooping cough with injection of maternal whole blood in a series of 62 cases is reported. It was efficacious in about 66.1 per cent and some improvement was observed in another 9.7 per cent of cases. Pregnant mother's blood was found more potent. A suggestion is made that some hormone, normally present in mother's blood and in greater amount during pregnancy, might be responsible for the curative effect in whooping cough.

INGUINAL HERNIAS

THEIR COMMONER VARIETIES AND OPERATIVE TREATMENT

Based upon a study of 109 cases

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SOME authors of textbooks on general surgery content themselves, in their chapters on inguinal hernias, with the generalization that there are two types of these, indirect and direct. After describing their main features, they indicate that the treatment of the former is the Bassini operation, which they describe without much detail, and, of the latter, some form of plastic repair.

The student thus often fails to gain a real grasp of the essential problems involved, both theoretical and practical; and the knowledge of the average young house surgeon on this subject is frequently vague. This article is an attempt to present the problems as clearly and simply as possible, and to indicate ways in which they may be tackled. The author's

interest in the subject was stimulated by reading Prof. Zimmermann's article in the *Surgery, Gynaecology and Obstetrics*, November 1940, Vol. 71, No. 5. The opinions expressed in the present paper are based on a small series of 109 cases of which full records are available, and on the experience of over a hundred more operations the case notes of which are not available. All the patients in both series were operated upon personally by the author.

Anatomy

The general anatomy of the normal inguinal canal is not discussed in detail here as it is described in textbooks, and in Zimmermann's article, from which it will be seen that the statements sometimes copied from book to book are incomplete and sometimes misleading. But the *precise* anatomy of each individual hernia is different, and must be studied at the time of operation in order to be able to remedy the particular defects present.

In studying any hernia, the important anatomical facts to consider are these:—

1. *Peritoneum.*—A protrusion of this through the ring of the canal forms the sac of an oblique inguinal hernia, and always lies in front of the cord. This constant position supports the theory of congenital origin, since such position can hardly be fortuitous. Another fact which supports this theory is exemplified in that every now and again the surgeon is called to see a patient in whom an inguinal hernia has become strangulated suddenly, but who denies absolutely the presence of any previous bulge or pain in the groin. The author has seen seven such examples, one in England, and six in India. In each instance the sac was fine and long, lying in the usual position, and adherent to the tissues round it. It is impossible to see how such a sac could come down from the peritoneal cavity in a second of time and thread its way carefully over the vessels and vas as far as the bottom of the scrotum, and finally become adherent to the tissues round it, and yet not show any evidence of trauma at operation an hour or two later. It is even more difficult to visualize the sudden descent of the sac in the case of a funicular type of hernia which becomes strangulated. The sac must be present from birth.

2. *The arching fibres of the internal oblique muscle.*—These act as a sphincter to the internal ring, and compress the neck of the sac and the cord whenever the abdominal wall contracts. In time, a ring of fibrosis is produced at the neck of the sac. The fibres are fleshy and so the term conjoint tendon is a misnomer. If the abdominal pressure is increased suddenly or repeatedly to such an extent that it overcomes the internal oblique sphincter round the internal ring, then part of the abdominal contents may be forced temporarily or permanently into the sac. This gives rise to the pain and lump in the groin which

is the patient's first evidence of the abnormality he has had from birth.

3. *The internal abdominal ring.*—This funnel-shaped opening in the aponeurosis of transversus abdominis is gradually stretched if the abdominal contents repeatedly come out and have to be returned. Later it becomes so dilated that the abdominal contents slide in and out with variations of abdominal pressure and bodily posture. The arching fibres of the internal oblique do not take part in the formation of the internal ring, but act as its sphincter.

4. *The external abdominal ring.*—In time, this also becomes dilated by the contents of the fundus of the sac. The fibres of the external oblique around it become very stretched out and thinned, and in time become somewhat atrophied.

5. *The fleshy fibres of the internal oblique which lie between the lateral edge of the rectus abdominis and the inguinal ligament.*—The congenital thinness or absence of these fibres is the reason for the occurrence of most direct hernias. This weakness is often not apparent till the muscles become flaccid in old age. The aponeurotic layer of the transversus abdominis is not in itself strong enough to withstand the constant strain of increased abdominal pressure in defæcation or in coughing, and so a bulge appears in the region of Hesselbach's triangle. Thus, a direct hernia is essentially different from an indirect hernia in that the muscle and not the sac is congenitally defective.

6. *Huge hernias.*—In the final stages of a large indirect hernia, especially where a truss has been applied, both the external and internal oblique muscles become atrophied to such an extent that the picture approaches that of a direct inguinal hernia. Both rings become coincident and enormously enlarged.

Thus, the normal inguinal canal in the male is an oblique tunnel in the abdominal wall for transmitting the spermatic cord. It has an excellent valvular apparatus at the inner end for preventing the protrusion of the abdominal contents. But the presence of a congenital protrusion of the peritoneum in this canal or the congenital absence of fleshy muscle over the Hesselbach's triangle, together with their sequelæ, give rise to our problems.

The individuality and aim of the operations.—There are both major and minor differences in the anatomy of inguinal hernias, but it must be stressed that every inguinal hernia is peculiar, and must be recognized and treated as such. It is for this reason that this article is entitled 'inguinal hernias, etc.', and not 'the treatment of inguinal hernia.'

Oblique inguinal hernias

The aim of the operations for the cure of oblique inguinal hernias is to remove the congenital abnormality, i.e. the sac, and to restore

to the canal its original size and range of activity wherever possible.

The most important objects to be accomplished are:—(1) Removal of the sac. (2) Narrowing of the stretched inguinal rings. (3) Avoidance of interference with the sphincter mechanism of the canal.

The method of repair of any inguinal hernia depends on its own peculiar anatomical features and not on the duration of the hernia nor on the age of the patient.—For example, every general surgeon has had the experience of dealing with some huge hernias in infants in which the rings are both widely stretched, and the sac is often widemouthed and of the funicular type. These require more operative interference than simple ligation of the sac which is advocated by some authors, if the canal is to be restored to its normal size and range of activity. So, before attempting to indicate the rational treatment of inguinal hernias, it may be repeated that, although there are some fairly well-defined groups of inguinal hernias for which there are recognized methods of treatment, yet each hernia must be treated on its own merits and must receive individual consideration and methods of repair.

A classification is given of the common types of inguinal hernias and the rational lines of treatment indicated.

Stage 1.—Hernias in which the sac is small and the rings are not enlarged. (In this series 7 cases—6.42 per cent.)

The operation of choice for hernias in this stage is the following:—

The operator first makes certain by superficial palpation that the external ring is not enlarged. An incision is made through the external oblique over the internal ring, and is continued downwards nearly as far as the external ring, which is left intact. The internal oblique is exposed and retracted laterally and upwards with an aneurysm needle inserted just over the internal ring. The cremasteric fibres overlying the cord are separated by blunt dissection and the internal spermatic fascia and cord are exposed. The cord and sac are gently separated from this fascia covering them, and isolated from each other. The cord is held out of the way by two pairs of Lane's tissue forceps, and the sac is dissected with gauze up to its neck at the internal ring. A purse-string suture is then applied around the neck of the sac, which is cut off half an inch distally and its stump allowed to retract. It is easy then to feel and inspect the internal ring which surrounds a finger placed over the retracted neck of the sac. If it is not stretched, all that remains to be done is to drop the cord into position and sew up the external oblique over it with three or four interrupted silk sutures, and stitch the skin. There is no need to touch the external ring. The advantages of this method, compared with the old practice of mere ligation of the sac without incising the external ring or the external oblique over the internal ring, are that, (1) a good view of the internal ring is obtained, and (2) the sac can be dissected throughout its full length.

Stage 2a.—Hernias which have become enlarged beyond stage 1, in that the rings have become slightly stretched. (In this series 7 cases—6.42 per cent.)

The previous operation can be performed with the modification that the internal ring can

be narrowed by a stitch, the external ring pillar can also be so dealt with, and the canal restored to normal with the minimum of trauma.

Stage 2b.—These are hernias of the funicular type, similar to those described in stage 3b, but with rings stretched only slightly. (In this series 5 cases—4.59 per cent.)

Stage 3a.—Hernias in which the internal and external rings are both moderately enlarged. (In this series 35 cases—32.11 per cent.)

This is the commonest stage encountered in India. The hernia has been present for some months or years. The constant piston-like backward and forward motion of the omentum or bowel through the internal ring at last overcomes the sphincter action of the internal oblique. (This sphincter action is most easily seen when an operation for inguinal hernia is proceeding under a badly given general anæsthetic. Whenever the patient strains, the internal oblique arching fibres are seen to contract down on the cord and sac, making operative interference difficult). The internal and external rings in turn become progressively enlarged, and the hernial contents glide easily in and out of the canal.

For hernias in this stage the following operation is a reasonable one :—

The external oblique is incised through the dilated external ring to a point above the level of the internal ring. The flaps of aponeurosis are held aside, and the fleshy fibres of the cremaster muscle overlying the cord are then split longitudinally. The internal spermatic fascia is similarly split. The sac is now exposed, its folded edge being usually identified with ease, and grasped with a pair of artery forceps. The two coverings of the sac which have just been split are now stripped off by gauze dissection aided by snips with the scissors to cut the harder strands of fibrous tissue. The cord is always found behind the sac and is similarly isolated from it as far as the internal ring. The cord is then dissected free from the tissues and is held up between two Lane's tissue forceps. This process is difficult and needs both care and delicacy, since it is important to avoid rupturing the veins of the cord, but it can be kept bloodless by using a finger covered with gauze for most of the dissection, and by employing scissors to cut only the relatively avascular fibrous strands.

It will be found that the vas and its accompanying vessel run in a separate fascial compartment from that containing the venous bundle. In order to avoid injury to the vas and its artery, they should be held up from the sac, slightly on the stretch, when the walls of the fascial tunnel in which they lie will be easily identified and can be slit up with scissors. The same method should be adopted when dealing with the veins of the cord, and will lead to a minimum of trauma and hæmorrhage, and to a saving of time.

The next procedure is to open the sac and ensure that none of its contents is adherent to the walls. If the contents are adherent, they must be separated and returned to the abdominal cavity. Adherent omentum often needs dividing, the proximal end being first transfixed and ligated. (The treatment of the relatively rare sliding hernias is not discussed here.)

The neck of the sac is surrounded by a purse-string suture, which is tightened after making sure that it does not include any of the abdominal contents. A purse-string suture is the surest method of obliterating the neck of the sac, which is divided half an inch distal to the suture. The stump is allowed to retract

and should not be stitched to the internal oblique muscle, as no useful purpose is served in doing so. The arching fibres of the internal oblique together with the cord are gently retracted upwards and laterally, and the internal ring can then be recognized visually or by a finger placed over the retracted stump of the sac. The ring should be narrowed by approximating its edges to each other with one or more silk sutures. No tension need be applied in doing this, as the fascial layer is lax and mobile. The stitch should not include the internal oblique fleshy fibres. The common practice of suturing the fleshy fibres of the internal oblique to the inguinal ligament is physiologically unsound for these reasons : (1) it has been shown that fleshy muscle does not readily unite with fascia; (2) any muscle when pulled out of its normal position will tend to return thereto, and (3) the sutures will therefore tend to cut through the muscle, especially if they are tied tightly, when their effect will also cause the muscle to atrophy. This procedure will tend, consequently, to hinder rather than assist the object of the operation.

The cord is then allowed to resume its normal position. When the cremaster muscle is well developed, as is often found, it is advisable to unite the split portions of the muscle with one or two loosely applied silk sutures, in order to include as few fibres as possible. This procedure covers the cord with muscle (as it was covered before the operation began) and renders it less liable to damage when suturing the external oblique over it. The external oblique is sewn up with interrupted silk stitches, and the external ring re-fashioned to its normal size.

By this operation the canal and rings are restored to their normal dimensions, and further interference is harmful and unnecessary. The only abnormalities were : (1) an embryonic sac, and (2) resultant stretched internal and external rings. These have been rectified, and no more needs to be done.

Stage 3b.—(In this series 15 cases—13.72 per cent.)

In this stage is included that common variety in which the processus vaginalis is widely patent and the testis lies in the fundus of the sac. It is common in infants and young children. The hernia is usually large and the rings stretched, yet the sac may be of very fine texture.

The operation necessary for this type is very similar to that described in 3a, except for the increased difficulty in dissecting the sac from the cord. The fundus of the sac is the testis and should not form the starting point of the dissection.

The cremasteric and internal spermatic fascial layers are split longitudinally as before, and the sac is exposed. It is found to be long and no fundus is definable. It is then incised longitudinally and the nature of the condition is fully established. The cord is seen shining through the peritoneum forming the posterior wall of the sac. The sac is carefully peeled off circumferentially from the cord by blunt dissection begun by inserting a closed pair of artery forceps between the two, and then opening its jaws. Sometimes the dissection is so difficult to carry out without tearing the fine sac that it is easier to incise the sac all round transversely from within. The proximal edges of the peritoneum should then be grasped, and an attempt made to separate the layers by blunt dissection. It is better to begin fairly low down towards the testis, because the peritoneum near the neck of the sac may easily be so torn in beginning the plane of separation that ligation of the neck of the sac may be made nearly impossible. A proximal sleeve of the peritoneum is thus dissected up to the internal ring, and there secured by a purse-string suture. The remainder of the sac can either be left as it is, inverted, or removed as far as

the testis. The former is the best method, especially in children. The tissues are less traumatized, and the occurrence of post-operative hydrocele due to leaving behind a large area of the peritoneum is not common. The operation is concluded as in 3a.

Stage 4.—Large hernias of long duration, especially those on which a truss has been applied, and in which the medial margin of the internal ring may be stretched as far medially as the pubic spine, and coincides with an equally large external ring. The muscles surrounding the rings have also become stretched and atrophied. (In this series 20 cases—18.35 per cent).

This state of affairs approximates to that seen in large direct hernias, and requires the same treatment.

Direct inguinal hernias

A. Small direct inguinal hernias.—(In this series 7 cases—6.42 per cent.)

The essential aetiology, the presence of a congenital muscular deficiency, has been discussed. This is based on the findings of Anson and McVay, and explains most of the cases met with in practice.

The logical method of curing direct hernias is to repair a broad hold in the fascial aponeurosis and to strengthen the area over it. Since it is not possible to make muscle grow over the area concerned, some reinforcing type of plastic fascial operation must be employed.

The sac is exposed as outlined in 3a and its wide neck secured by a purse-string suture. The fundus of the sac, if it is small and dome-shaped, can be either inverted or stitched to itself to produce obliteration. The transversalis fascia is then stitched to the inguinal ligament over the sac, and the previous size and form of the canal are reconstituted. But as the previous structure of the canal was congenitally unsatisfactory, the deficient fascio-muscular layers must be strengthened by one or more layers transplanted from elsewhere.

There are many types of plastic operation performed nowadays, the most successful being those in which no attempt whatsoever is made to pull tissues together under tension:—

(a) Zimmermann uses part of the lower flap of the external oblique which he stitches across under the internal oblique. In the author's experience, this has been a good method where the direct hernia is small and the external oblique has become atrophied, but it has been found useless in some of the large direct hernias discussed later.

(b) Some surgeons (e.g. R. Maingot) used an interlacing darn of floss silk sutures which is said to provoke a strong fibrous reaction in the tissues. This method has undoubtedly proved effective in expert hands, but the author has had no experience of it.

(c) Others use a turned or sliding flap from the rectus sheath in order to cover up the

defect. This method is also not used by the author.

(d) The operation which the author prefers for congenital direct hernias is that in which fascial aponeurotic grafts are taken from the tensor fascia lata aponeurosis of the thigh by means of a Moseley's fasciotome, and are applied with an interlacing darn over the transversus aponeurosis to fill in the triangular gap. There is no tissue brought under tension, and a thick layer of fascia is applied. There is little post-operative pain. The operation takes both time and much trouble and requires a scrupulous aseptic technique from beginning to end.

Moseley's fasciotome is simple and effective, cutting an adequate graft with one manipulation through one small incision. The graft can be split longitudinally into two or three narrower pieces, as required. The thigh from which the grafts are taken should be firmly bandaged at once from the groin to the knee to prevent the occurrence of any subcutaneous hæmatoma. The author has had no complaints of pain in the leg after removal of the graft and no instances of hæmatoma.

Gallie's needles are used to apply the fascial darn which is secured by means of silk sutures to prevent slipping. The stitches should extend from the inguinal ligament vertically up and down from the internal ring to the pubic spine until the area is covered, when the horizontal interlacing stitches should be applied. Great care should be taken in every detail as to the insertion of the fascial sutures. The author has seen the complication of femoral venous thrombosis due to lack of care in inserting one of the vertical stitches under the inguinal ligament. The operator should leave himself ample time for the accurate insertion of every stitch. This may sound an obvious statement, but it is not always implemented in practice. The operation is concluded by dropping the cord into position and after covering it with the cremaster muscle, sewing up the external oblique over the cord.

B. Medium and large direct hernias.—(In this series 13 cases—11.92 per cent.)

The operative treatment of large direct hernias and of oblique hernias may be accomplished by method (d) just outlined. These large hernias, however, usually have thick and strong sacs covered with a thick layer of transversalis fascia aponeurosis.

Accordingly, the sac and its fascial covering are dissected up as far as the margins of the concurrent internal and external rings, and it then becomes evident that, instead of being wasted, this tissue will make exceedingly good grafting material for reinforcing the triangular deficiency between the inguinal ligament, rectus sheath, and internal ring. The next step in the operation is to occlude the neck of the sac with a purse-string suture either from the outside or inside of the sac. The author has found that the insertion of two sutures at a distance of $1\frac{1}{3}$ inch from each other is better than the use of only a single suture, because a short, thick fibrous cord is produced at the neck of the sac, which occludes it well.

The body of the sac can now be used for the fascial repair in a variety of ways depending on the individual characteristics of the inguinal canal, the size of the sac, and the versatility of

the surgeon. Here again, it may be emphasized that there is no standard method of repair. Every hernia demands its own operation.

The following have been found in practice to be the best methods of using the sac as grafting material:—

(1) The sac is removed distal to the purse-string sutures and cut into narrow strips. This is most easily done by first splitting the sac longitudinally and then cutting the grafts from the circumference of the oblong piece of tissue. These strips are threaded on Gallie's needles and carefully darned over the required area as described in A(d) above. The author has found this method most successful, and it saves having to cut a graft from the leg. This method has been used only in 9 instances so far, but it deserves a wider trial.

(2) The sac is not removed, but is cut longitudinally into two or three broad strips which are used to overlap each other in various ways according to the peculiar weakness of the parts to be covered. Sometimes one flap is threaded through a slit made in the base of another; sometimes the flaps are stitched across each other and then back again. The weak area can usually be covered by a mass of fibrous tissue several layers' thick from the rectus sheath to the internal ring and the pubic spine. No tissues are pulled under tension in anyway. The cord is allowed to fall into place and the external oblique sewn over it as before. This method has been used in 19 instances and has been found extremely useful.

In a few of the cases in this group, the sphincter action of the internal oblique is almost non-existent owing to the size and duration of the hernia and the fibrous reaction produced by the wearing of a truss. Where it is found that the arching fibres of the internal oblique are obviously fibrous and atrophic, there is no point in attempting to conserve their minimal sphincter action. It is therefore rational to narrow the internal ring before the darning or repairing process begins by using any of the available muscle or fascial layers, since all are atrophic and will stretch to some extent, having lost their natural function. No tension must be employed.

Comments on some of the commoner complications of operations on inguinal hernias

1. *Sepsis.*—The reasons for this are well enough known, and the risk is increased in the longer operations involving the use of grafts. It is the experience of many that sulphonamide powder and 1/1,000 proflavine lotion introduced into the wound before sewing up reduce the incidence of sepsis.

2. *Edema of the scrotum.*—This is best avoided by strict adherence to the old rule which states that the operator must be able to pass the tip of his little finger into the re-fashioned ring. The rule applies to both internal and external rings.

3. *Hamatoma of the scrotum.*—Any slight oozing from a torn vessel in the cord may give rise to a collection of blood and serum in the scrotum, especially when the rule mentioned in 2, has not been observed. Obviously, if a vein has been partially obstructed, it will bleed more; and perhaps bleeding may begin again

in several places which were oozing slightly at operation, but had stopped before the insertion of the stitches. No advantage is gained by inserting a rubber glove drain to avoid this complication. Careful dissection of the cord and avoidance of any desire to 'stitch it up good and tight' are the best methods of prevention. The treatment is aspiration which may have to be repeated more than once. If the blood has clotted, the scrotum should be incised with full theatre technique, the clot removed, and the origin of the bleeding stopped. Some sulphonamide powder should be inserted before closing the wound.

4. *Hydrocele.*—This is rare, but when it does occur, it can be easily treated by aspiration, and soon subsides.

5. *Chest complications.*—After operation, the patient should be allowed to sit up, if he so desires. There is nothing more distressing than to see a patient, with a severe attack of bronchitis, who is compelled to lie flat on his back for three weeks after the operation in order to satisfy the whims of his surgeon. The increase in abdominal pressure due to prolonged bouts of coughing is surely more than that due to sitting up in bed.

6. *Recurrences.*—

(a) *In oblique inguinal hernias.* These may be due to one or more of several causes:—

(1) The neck of the sac may not have been properly dissected out and ligated. The ligature may have slipped, or the knot may have become untied. A purse-string suture should always be used.

(2) The internal ring may not have been narrowed sufficiently carefully, or not at all, thus leaving an obvious weak opening.

(3) The external ring may have been re-fashioned directly over the internal ring, thus leaving a direct channel for the abdominal contents to come out to the surface. This method of repair should now be condemned as unnatural and also unmechanical.

(4) Unnecessary interference with the sphincter mechanism of the canal, resulting in atrophied and fibrous tissues. This is often combined with 2.

(5) Attempts to pull tissues together under tension.

(b) *In direct inguinal hernias.* These occur because a sufficiently strong wall of tissue has not been placed in front of the bulging area. Here again, it is stressed that each hernia is a separate entity and the reasons for the recurrence of one may be different from those of another, although both have been repaired similarly. Insufficient regard to the individuality of any one hernia, and the performance of a stereotyped operation on differing kinds of direct hernias are important causes of recurrence. Another common cause is the attempt to pull tissues together under tension during the repair. Initially it may appear that a firm repair has been effected, but the

mistake will be realized later on when the ill-treated tissues stretch and atrophy, or the stitches cut through.

The author of this article has heard indirectly that three or four of the first 70 odd cases which he did in England by varying methods have recurred, but figures are not available.

Since coming to India, he has seen three cases of recurrence in those operated on by him, but unfortunately the full notes of these have been lost.

One was a case in which the external oblique muscle had been sutured under the cord, and the two rings were superimposed. At operation, it was found that a fine sac had gradually worked its way through the rings to the surface of the muscle layers. It was repaired as in 3a.

The second recurrence was one which was found to have been repaired by stitching the super-medial edge of the internal ring to the inguinal ligament after excision of the sac. However, the hernia had recurred through a part of the ring which had not been noticed, and which lay above the cord. The hernia bulged down over the previously-repaired portion of the ring. The internal ring had not received sufficient examination at the first operation.

The third instance was a large direct hernia in a goatherd. The size of the original hernia had been that of a large grape-fruit, and had, it is thought, been repaired by some form of flap sac grafting, but as the man refused re-operation on the ground that his recurrence was not big enough, the cause of recurrence remains unknown.

Discussion

It is a common enough experience when asking surgeons their method of treating inguinal hernias to hear such conflicting statements as: 'I always do a Bassini', or 'I never interfere with the canal. I just pull out the sac and ligate it', or 'I always do a fascial graft'. The surgeons represented by these statements are too apt to regard hernias *en masse*, and do not pay sufficient regard to the peculiarities of each individual case.

The fact that a large number of Bassini operations are successful has tended to produce in many surgeons an attitude of complacency with regard to their technique and results. This article is an attempt to outline the rational procedures of operation for the commoner types of inguinal hernia, and to stress the study of the anatomy and treatment of each individual example.

Summary

1. The article is based on a series of over 200 cases of inguinal hernia personally operated on.

2. There is no standard operation for the cure of inguinal hernias. Every hernia demands

its own (not the surgeon's own) operation based upon a careful study of its anatomy.

3. An attempt is made to classify the commoner types of inguinal hernias and to suggest methods of dealing with each.

4. It is suggested that the Bassini operation be abandoned in favour of more rational and physiological methods.

5. In the treatment of some types of large direct and indirect inguinal hernias, the use of the hernial sac and its immediate fascial covering as an excellent grafting material is mentioned. It is hoped that a wider trial of this method may be made and its merits or drawbacks assessed.

6. Some of the commoner complications of the operations are discussed and their treatment outlined.

7. A plea is made for a less stereotyped and complacent attitude towards the whole subject of inguinal hernias.

SYNERGISTIC EFFECT OF SULPHANILYL BENZAMIDE ON *V. CHOLERA* BACTERIOPHAGE

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FROM this laboratory De and Basu (1938) noted that sulphanilamide exerts a synergistic effect on the staphylococcus antitoxic and antibacterial serum in the treatment of staphylococcal infections. In the year 1939 Zaytzeff-Jern and Meleney again observed that sulphanilamide derivatives do not interfere significantly with the lytic action of specific bacteriophage. Accordingly, it was also considered to be of interest to study whether a sulphanilamide drug may exert a similar synergistic effect on any specific bacteriophage. From the belief that cholera phage is not so effective in clinical application the influence of sulphanil benzamide on the lytic action of specific bacteriophage of *V. cholera* has been studied. This sulphanilamide drug has recently been shown by Bose and Ghosh (1944) to be easily absorbable and not to exert any undue toxicity.

Little work has been done on the bacteriostatic action of sulphanilamide derivatives against *V. cholera*. In searching the literature it has been noticed that only very recently Sadusk and Oswald (1943) undertook to determine the effect of sulphathiazole, sulphadiazine, sulphaguanidine and sulphanilamide upon *V. cholera* growing in media free of inhibitor to these drugs. The compounds have been found to exert a bacteriostatic action in the descending order as recorded above. In this paper, certain bacteriostatic action of sulphanil benzamide against *V. cholera* and its influence on its bacteriophage

has been studied, and experimental observations are being recorded in this paper.

Experimental

Sulphanilyl benzamide, m.p. 181° , is a fine crystalline powder. Its solubility in water at 37.5°C . is 30 mg. per 100 c.cm.; but being readily miscible in alkaline solution, one gramme of the drug could be easily dissolved in 100 c.cm. of water at pH 8.0. Such a dilution of the drug was used throughout the present investigation as a stock solution.

Bacteriostatic action.—At first the bacteriostatic action of the drug against *V. cholera* was studied. The organism used was a smooth, partially susceptible laboratory strain of *V. cholera* (Inaba 2812). Stock cultures were always maintained in alkaline agar medium at pH 8.2. Different inocula from suspension in broth from a 18 hours young culture in agar were used to study the inhibitory power of the drug for a definite period of time in a medium made up of the usual papain digested meat broth. 0.05 c.cm. of the stock solution of sulphanilyl benzamide was added to 5 c.cm. of the broth in each case, and it was noted that the drug exerted its characteristic bacteriostatic action when the number of cells inoculated were up to 210 million or below (table I).

TABLE I
Bacteriostatic action of sulphanilyl benzamide :
Each tube contained 5 c.cm. broth; Drug concentration: 10 mg. per cent; Inoculum: Broth suspension from 18 hours young agar culture

Number of cells inoculated in million	Growth after hours		
	24	48	72
35	—	—	—
70	—	—	—
105	—	—	—
175	—	—	—
210	—	—	—
245	—	—	—
280	—	—	—
Culture control	+	+	+

+ Growth. — No growth.

It was then considered necessary to find out the concentration of the drug that would not exert any bacteriostatic action under the conditions of the experiment. It has been observed that in a dilution of 1:20,000 the drug exerts no bacteriostatic action even with a smaller amount of the inoculum.

Action of the drug in presence of *V. cholera* phage:—

It was noted that partially susceptible strains of *V. cholera* were destroyed by the lytic action of its stock bacteriophage *in vitro*: on further incubation they gave rise to some secondary growth after 24 hours. This did not undergo

lysis by addition of any further quantity of the stock bacteriophage. To find out whether this secondary growth could be prevented by incorporating sulphanilyl benzamide in a concentration (1:20,000) that did not exert any bacteriostatic action on the organism, the following experiments were carried out:—

A.—A set of tubes each containing broth (5 c.cm.) were inoculated with 35×10^6 cells of the organisms and incubated for a definite period.

B.—A set of tubes each containing broth (5 c.cm.) and organisms (35×10^6 cells) were incubated as above after addition of 2.5×10^{-4} gm. of the drug (drug concentration 5 mg. per cent).

C.—A set of tubes each containing broth (5 c.cm.) and organisms (35×10^6 cells) were subjected to the lytic action of stock cholera bacteriophage as usual.

D.—A set of tubes each containing broth (5 c.cm.), organisms (35×10^6 cells) and the drug (2.5×10^{-4} gm.) were again subjected to the lytic action as above.

The results of the experiments are recorded in table II.

TABLE II
Media: Papain digested meat broth; Inoculum: 18 hours young agar culture; Drug concentration: 5 mg. per cent; Phage: Stock cholera phage of 10^8 concentration

Experiment	Appearance in tubes after hours				
	2	4	24	48	72
A (control culture)	+	++	++	++	++
B (drug 1 : 20,000)	+	++	++	++	++
C (phage action)	+	+	+	+	+
D (phage in presence of drug).	+	—	—	—	—

+ Growth.

— Lysis.

Action of the drug after secondary growth:—
To show that the drug acts only on those organisms that have escaped the lytic action of the specific bacteriophage and have appeared in the tube after 24 hours (*vide* experiment C in table II), two tubes each containing 5 c.cm. broth and organisms (35×10^6 cells), were subjected to the lytic action of stock cholera bacteriophage in the usual way. One tube was kept as control; to the other tube the drug (2.5×10^{-4} gm.) was added just on the appearance of the secondary growth after lysis. Both the tubes were then incubated for a definite period. It was observed that the tube containing only the drug showed no further growth and a complete lysis occurred subsequently as shown in table III.

The organisms that survived the lytic action of the specific bacteriophage were, on culture,

TABLE III

Inoculum: 18 hours young agar culture; Drug concentration: 5 mg. per cent; Phage: Stock cholera phage of 10^8 concentration; Media: Papain digested meat broth

Experiment	Appearance in tubes after hours				
	2	4	24	48	72
Broth <i>V. cholerae</i> phage.	+	—	+	+	+
Do.	+	—	+	—	—
			Drug added.		

found not to differ apparently from the original strain as regards their morphology and smoothness. They were also not affected by the drug in concentration of 1 in 20,000 as was previously noticed.

Discussion

From table I it would be evident that sulphanilyl benzamide exerts some bacteriostatic action on *V. cholerae* in papain digested broth; the organisms, however, growing in the medium when the concentration of the drug falls to 5 mg. per cent (dilution 1 in 20,000). In accordance with the observations of Zaytzeff-Jern and Meleney (1939), we have noted that this drug also has no destructive action on the lytic power of the particular cholera bacteriophage used. The experimental observations as recorded in table II tend to show further that the addition of the drug to the usual phage-bacterium medium helps in the complete inhibition of the growth of the secondary organisms. It would again be evident from the results as recorded in table III that the drug acts particularly in helping the bacteriophage in completely lysing the secondary organisms. The organisms found after the preliminary lytic action of bacteriophage are in all respects pure strains of *V. cholerae* except that they have become resistant to the action of the stock bacteriophage. These secondary organisms, as usual, were resistant to the bacteriostatic action of the drug in a concentration of 1:20,000 (5 mg. per cent). All the experiments so far carried out, prove that sulphanilyl benzamide exerts a synergistic action on the lytic power of cholera bacteriophage.

Summary

1. Sulphanilyl benzamide in a concentration of 1:10,000 exerts bacteriostatic action on a suspension of *V. cholerae*; a higher dilution than this shows a free growth of the organism.
2. The lytic action of the cholera bacteriophage seems to increase in presence of the drug.
3. In view of the observations recorded, it may be suggested that a treatment with specific

bacteriophage combined with sulphanilyl benzamide may be clinically useful in cholera patients.

In conclusion, the authors wish to express their sincere thanks to Mr. P. Sen Gupta, M.Sc., for his valuable suggestion during the course of this investigation.

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TUBERCULOSIS OF THE SKULL

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TUBERCULOSIS osteitis of the skull is not common, and, when it is met with in the absence of frank signs of tuberculous disease of the lungs or lymphatic glands, it is likely to provide a diagnostic conundrum, as has been exemplified by the following case.

A Madrassi soldier, aged 21, was admitted to hospital for fever accompanied by a soft fluctuating swelling about the size of an egg over the ninth left rib in the anterior axillary line. The swelling was neither hot nor reddened. The patient was of rather poor physique and gave a history of 'clinical malaria' six months previously and common cold a month later, but had otherwise been in good health. X-ray examination was carried out, and a localized area of bony destruction with no change in size was seen in the ninth left rib with a parallel deposition of sub-periosteal bone, and some small granular sequestra (see figure 1, plate VI). There were no obvious signs of disease in the lungs, and the sputum was repeatedly negative for tubercle bacilli; the Kahn test was repeatedly negative.

A small swelling was seen over the lateral part of the left eyebrow in the usual site of, and clinically very much resembling, a dermoid. Under this swelling radiological examination of the skull (see figures 2 and 3, plate VI) revealed a punched out area of erosion of both tables in the frontal bone and an unsuspected second punched out area in the left parietal bone over which a small swelling was seen only when the hair was shaved. A puffy swelling was found between the spine and the lower half of the medial border of the left scapula. X-ray examination of this region showed no bony changes, and no fluid could be aspirated.

The swelling over the ninth rib yielded fluid resembling ordinary pus, and blood-stained

fluid was withdrawn from the swelling in the left frontal region. In each case, the fluid on examination was sterile and microscopically consisted of amorphous debris with degenerating pus cells. Four weeks later, a serous effusion appeared in the right chest; this was aspirated, but no organisms were recovered from it.

Blood examinations revealed 4,020,000 red cells and 11,600 leucocytes per c.mm. (polymorphonuclears 55 per cent, lymphocytes 29 per cent, mononuclear cells 10 per cent and eosinophils 6 per cent), hæmoglobin 10 grammes per 100 c.cm., the sedimentation rate was 95 mm. in first hour.

At operation, the ninth rib was exposed under pentothal anæsthesia and the diseased area was resected. Material resembling ordinary pus was mopped away, and the wound was sutured after the introduction of about a drachm of pure urea. The wound healed by primary union.

Ten days later, as the swelling in the frontal region had repeatedly refilled after aspiration, and the skin was becoming unhealthy, a flap enclosing the area was turned down, an abscess penetrating the temporal fascia and muscle was opened up, and the frontal bone exposed. A ring of diseased bone was excised with a chisel. Urea was inserted and the wound was closed (see figure 4, plate VI). Some sloughing of the previously unhealthy skin occurred, but otherwise the wound healed by primary union. The patient continued to run a low fever, but said he felt quite well. The abscesses were never more than slightly tender. Histological examination of the removed portions of bone revealed tuberculous disease, and guinea-pig inoculation was positive for tuberculosis.

Commentary

The patient had complained of only fever and soft swellings over the chest, skull and left scapular regions. Apart from a right pleural effusion and a high sedimentation rate there was little to confirm a provisional diagnosis of tuberculous caries of the rib and skull.

Tuberculous disease of the cranial bones is very uncommon, and more usually it is either secondary to a meningeal focus or to extension from cervical vertebræ or tuberculous middle ear disease. In this case it appeared to have originated in the diploë. The involvement of the inner and outer tables was equal in extent; the dura showed little more than irritation, and the pus had not burrowed between the bone and the dura at all. The x-ray appearances were suggestive though not absolutely pathognomonic of tuberculous disease, and it was therefore necessary to exclude other inflammatory bone diseases such as typhoid, and low-grade pyogenic osteitis and syphilitic disease, as well as both primary and secondary neoplastic conditions. The diagnosis was finally established by histological examination of the

removed portions of diseased bone and by guinea-pig inoculation. In this case the bone disease was probably blood borne from a focus in the right lung which was recognizable neither clinically nor radiologically until an effusion developed. There was no obvious enlargement in any of the superficial lymph nodes.

Acknowledgment

Permission to publish this article was kindly accorded by Brigadier W. Foot, D.B.M.S., of a Force.

DEHYDRATION TREATED BY CONTINUOUS GASTRIC DRIP

By A. C. MOLDEN

CAPTAIN, I.A.M.C.

THE problem of the dehydrated patient is a very real one, and dehydration occurs far more commonly than is realized, particularly in tropical and sub-tropical countries.

The normal daily fluid loss from the body in a temperate climate, through the lungs, skin, urine and faeces, is approximately $4\frac{1}{2}$ pints. In hot countries the urine output is lower, but evaporation from the skin is greatly increased and the daily total loss is 6 pints or more. Loss of fluid from the body continues even if there is no fluid intake, approximately $2\frac{1}{2}$ pints being lost daily in a temperate climate, in the absence of any intake. When fluid loss exceeds intake, tissue fluids are reduced, and this constitutes dehydration. Later, hæmoconcentration occurs, and the urine output having dropped to an amount too small to carry off all the waste products, toxæmia and delirium result.

Dehydration occurs most frequently in prolonged high fevers, persistent vomiting, and prolonged diarrhœa and allied conditions. Examination of such patients will invariably show a dry tongue and oliguria, and later, a low blood pressure and feeble pulse. These signs indicate a loss of from 6 to 9 pints or more of body fluid, for no clinical dehydration occurs before a loss of $4\frac{1}{2}$ pints of tissue fluid has occurred.

The importance of dehydration receives fresh and added significance with the advent of the sulphonamide drugs, particularly sulphapyridine, sulphathiazole and sulphadiazine. These drugs are liable to be deposited in the renal tubules, renal pelvis or ureters causing anuria or hæmaturia when the secretion of urine falls below 500 c.cm. (17 fl. oz.) daily. To prevent this symptom-complex, a secretion of urine amounting to 1,500 c.cm. (50 oz.) daily is required (*M. R. C. War Memorandum, No. 10*).

The methods formerly used for the active treatment of dehydration were, in addition to encouraging the intake of fluids by mouth when possible, subcutaneous injection of saline, and the giving of fluids by rectum. Both these methods still have their uses, but both have given place to other methods. Subcutaneous injections of saline are particularly useful for infants, but

are quite inadequate for the really dehydrated patient. In devitalized tissues, their continued use may lead to abscess formation despite meticulous care in regard to asepsis. A better but similar method is continuous intramuscular saline (Bailey, 1942). Rectal salines are given by slow drip, or intermittently. Murphy advocated the giving of rectal salines by slow absorption from fluid in a can not more than one foot above the rectum and connected with the latter by a wide-bore tube so that bowel gases could freely escape. He taught that large quantities of fluid could be absorbed by this means. The method is excellent in all but practice. Sooner or later, and sooner rather than later, the method comes to grief in a soiled bed and is never popular with the nursing staff.

In 1934, Bailey and Carnow popularized in England the practice, already adopted in Canada, of giving salines by continuous intravenous drip. The following ten years have seen an enormous use of intravenous salines, until now, Bailey himself says that vigilance is required in order to curtail its use (Bailey, 1944). There is no doubt about its being a life-saving procedure, but it is not without its disadvantages and dangers. It is well known that the circulation has frequently been overloaded, and pulmonary oedema and death have occurred. Patients have been drowned, as it were, in their own fluids. The infusion fluids have to be very carefully prepared and sterilized, using pyrogen-free water.

Recently, use has been made of the bone marrow for saline infusion (Bailey, 1944), particularly in children (Gimson, 1944). The method is open to criticism that bone infection may possibly occur with devastating effects. It is however a practice which will increase.

The purpose of this article is to commend the advantages of giving fluids by continuous gastric drip, or oesophageal drip. Nasal feeding has been long employed, and continuous gastric drip is an elaboration of nasal feeding. Nasal feeding has been used intermittently for the administration of nutriment. The procedure now to be described is the giving of fluids continuously by drip.

Apparatus.—The apparatus used includes a glass receptacle for fluid, tubing with controlling clamp, glass drop counter as used for intravenous infusion, and a Ryle's tube. Experience has shown that a Ryle's tube is preferable to the shorter catheter employed for nasal feeding, though the latter may be used.

Technique.—The nostril is cleaned and the Ryle's tube, having been previously dipped in water or smeared with lubricant, is gently introduced. There is usually transient discomfort as the tube passes the region of the larynx. At this stage the patient, if able to be sufficiently co-operative, is given a sip of water to drink and the tube is advanced during the act of swallowing. This effectively prevents the tube entering the larynx. Alternatively the patient is told to

breathe slowly and deeply and the tube is advanced during expiration. There is no suggestion of trouble at this stage in the drowsy or unconscious. When the tube has been introduced as far as the first or second mark, it is attached to the forehead by adhesive tape, and connected to the drip apparatus. It is advisable to wait for a few moments before beginning to administer fluids in order that the patient may become accustomed to the tube.

The rate of flow for continuous use is 40 to 60 drops per minute, which is equivalent to 6 to 9 pints per day, but strict accuracy in this is not required. Fluids given by continuous drip is tolerated better than larger quantities intermittently. At the beginning, if dehydration is marked, 90 drops per minute is satisfactory and easily tolerated. Sufficient is given to maintain an excretion of about 50 fl. oz. of urine daily, as this is the only way by which one knows that the intake is adequate.

A variety of fluids may be used but, as salt is lost with all the body excretions, the best fluid to use is one containing salt. Half a teaspoonful of salt dissolved in one pint of water, or glucose water, is satisfactory. In certain conditions, sodium bicarbonate solution, one drachm to the pint is useful. Where feeding is required, citrated milk may be used. In addition, any medicines which have to be given orally may be added to the receptacle.

The advantages of this method over others of combating dehydration are many. Fluid is absorbed in a natural manner from the stomach. This may not be said of fluids introduced by intravenous, subcutaneous or bone marrow routes. There is consequently no necessity for sterile fluids to be used; ordinary, clean, potable water is the basis. The technique is simple and does not always require the presence of a doctor, but may be carried out by a nurse. Once it is started it does not require the same degree of expert attention as is required in intravenous infusion. This is of importance when the staff is not fully trained, or is small. Should the giving receptacle become empty no harm is done and there is no canula or needle to become blocked thereby. There is a much greater range of rate with which the fluid may be given with safety than is the case with intravenous fluids. There is much less effort involved than when fluids by mouth are urged upon an unwilling patient; many patients with the best of intentions find it difficult to drink the large quantities of fluids required to maintain an adequate diuresis. There is no risk of sepsis or of pulmonary oedema. The intake by mouth may be augmented as the patient feels inclined. Experience and theory indicate that it is far better to give fluids continuously by drip, than larger quantities intermittently as in ordinary nasal feeding. Distention of the stomach, a sense of fullness and nausea are entirely avoided and ultimately a much greater quantity is absorbed. It is not suggested that there is no discomfort, but it can be tolerated

for days and is less irksome than intravenous salines continued for a similar period. It is easy and so is likely to be given early.

The limitations are also obvious, and it is by no means suggested that it should replace intravenous infusion entirely; but where the method is applicable, it is far preferable, as the natural process of absorption is followed and when given early in sulphonamide therapy removes the risk of anuria and hæmaturia. The main limitation in a case where it is otherwise considered applicable, is vomiting. On the other hand, once the tube is introduced, vomiting, which was previously present, may cease. Vomiting is frequently induced by the act of swallowing, and does not occur when fluid is introduced by drip. This point is well brought out by the following example:—

The patient, a man aged 25, was received in a mildly dehydrated condition, suffering from blackwater fever. Notes which accompanied him stated that throughout the day he had vomited all that he had taken. As the Ryle's tube was being introduced he vomited bile stained vomit, but the tube was introduced without difficulty. From this time onwards no vomiting occurred and in the next 24 hours nine pints of bicarbonate of soda solution were given effecting an adequate diuresis and cure of the condition.

The following are types of patients on whom the method has been used with success. The very ill who are undergoing treatment with sulphapyridine or sulphathiazole. In some of these, no matter what efforts were made to enforce an adequate intake of the fluids by mouth, the excretion of urine frequently amounted to no more than 12 oz. in 24 hours. Often an intake of 8 pints daily is required to produce an excretion of 50 oz. of urine. Gastric drip has proved an invaluable method of giving fluid to cases of cerebral malaria who have not responded readily to intravenous quinine and who are drowsy for a considerable period. Alkalies may be given to such patients by this route. In blackwater fever, as in the case mentioned above, it is the only method by which large quantities of bicarbonate of soda solution may be given easily. In high and prolonged fevers where classical dehydration with dry tongue, oliguria, low blood pressure and feeble pulse are most frequently seen, it is of inestimable value. It has also been used post-operatively when the need for fluid was obvious and great. There is a wide scope of usefulness in post-operative and surgical work for fluids given by this method. Finally, in severe enteric and allied conditions when adequate nutrition cannot be maintained by ordinary feeding, milk may be introduced by this way as a nutrient fluid.

Summary

The frequency of dehydration in hot climates and its special importance following the introduction of sulphonamide therapy has been stressed. The features of dehydration and the methods in vogue for the treatment of this condition have been briefly reviewed. A method of

treating dehydration by continuous gastric drip, using a Ryle's tube, has been described and its many advantages enumerated. Some commendation of the method may be inferred by the enthusiasm shown by the nursing staff, and I have been encouraged to report the use of this procedure by noting its spontaneous use by fellow medical officers.

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REPORT ON AN EPIDEMIC OF SCRUB TYPHUS (K FORM) TREATED AT A GENERAL HOSPITAL IN BURMA*

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DURING September, 1941, 107 cases of this disease were received in a hospital. These patients started coming in from the 2nd; there was one on that day and one again on the 7th; the number increased to 3 on the 9th and from the 11th patients came in increasing numbers up to the 20th; on the 21st there were only 3 and on the 25th only one, and the admissions ceased.

Out of these 107 cases, 105 were from one unit camping in a rural area; out of the five companies of this unit, one company escaped the disease excepting for five members who were doing duty with the other companies. Two other cases were from another camp about 13 miles from the affected one and belonged to different units, but these men had visited the affected area.

Signs and symptoms.—Fever, headache and slow pulse were present in all cases, and the tongue thickly coated with brownish fur was usually a prominent feature. The fever lasted for more than 18 days in 19, between 13 and 18 days in 60, and for less than 13 days in 28. The fever usually came down by lysis. In some cases after coming to normal it became intermittent for a few days.

In 88 cases, there was enlargement of lymph glands with or without tenderness. The enlargement was general in some cases and in a group of glands in some cases; in the latter, it was usually the group associated with the area of the necrotic patch.

Pains all over the body, a 'mousy' smell and drowsiness were found in about 60 cases. A macular rash was seen in 30 cases, and a papular rash in 8. The rash usually appeared

* Paper rearranged by the editor.

between the 3rd and 5th day of disease and disappeared within 48 hours. It was mostly on the trunk.

A necrotic patch or 'bite mark' was seen on the chest or shoulders in 19, on the trunk in 11 and on other parts of the body in 8. The patch was 2 to 3 mm. in diameter, round, dark, tough, firmly adherent, covered with a scab and surrounded with areola. It was present up to a week or ten days after the onset. In some cases more than one patch were seen.

Other symptoms noted were enlarged spleen in 29, injected eyes in 21, epistaxis in 7, and vomiting or pain in the abdomen in 3.

Diagnosis.—The following examinations were done for confirming the diagnosis.

(i) Total leucocyte count. In 42 cases, this ranged from 9,000 to 13,500 per cm.; in most cases it was low or normal at first but rose at the end of the first week.

Leucopenia (5,000 or below) was present in 12.

(ii) Differential counts. Lymphocytosis (above 35 per cent) was found in 59 cases.

(iii) Weil-Felix reaction.

for a week after which they were allowed to walk. They were discharged after 3 to 4 weeks and sent to a convalescent camp and were recommended two weeks' excuse duty and 3 weeks' light duty.

Out of 107 cases, two died.

Relapses.—Textbooks make no mention of a relapse in scrub typhus. In this epidemic, 10 out of 107 cases showed relapses. In some the temperature having come to normal remained so for 4 to 5 days after which there was a relapse lasting for 4 to 5 days; in others the temperature after being normal for a day or so started an intermittent course for 4 to 5 days.

Discussion.—Clinical and laboratory findings show that this is an epidemic of mite typhus as described by Manson-Bahr after Megaw's classification; this is usually not epidemic (synonyms—Tsutsugamushi fever, Shimamushi, exanthematous glandular fever, scrub typhus or 'K' form). Lewthwaite and Savor (1936) completely identified scrub typhus with Japanese river fever. Anigstein (1933) demonstrated the rat to be the normal

TABLE

RESULT OF WEIL-FELIX REACTION SHOWING THE MAXIMUM TITRE IN 107 CASES

With OXK						Those also showing agglutination with OX2 OX19		
1 in	1 in	1 in	1 in	1 in	1 in	1 in	Titre varying from 1 in 40 to 1 in 320	
80	160	320	640	1,280	2,560	5,120	10,240	
2	1	7	12	25	19	30	11	16

In all cases, the urine showed no albumen or any other abnormality.

Treatment.—The treatment was symptomatic. On admission, calomel followed by magnesium sulphate was prescribed, and a diaphoretic mixture was given for ordinary cases. In very toxic cases, with high fever, drowsiness, etc., one pint of normal saline per rectum was given and repeated if necessary six-hourly. In 16 cases showing rigidity of the neck and a positive Kernig's sign, lumbar puncture was done and some fluid was withdrawn. Other signs were treated symptomatically.

During the course of the fever, milk was given with ample fluids such as fresh lemon juice, lemonade and soda water. Milk was given four times a day, the daily total being 3 lbs. A pint of fresh lemonade three times a day was given as a routine. After the temperature had remained normal for a day or two, the diet was gradually increased to convalescent diet and then to ordinary diet.

Convalescence proved slow, there being great emaciation. In some cases the loss of weight was over 50 lbs. Patients were allowed to sit up in bed 4 days after fever, then in a chair

host in endemic typhus. It is generally recognized to be conveyed by a mite *Trombicula deliensis* which infests the rank vegetation, coarse grass, dead palm flowers and ears of rats. It is not ordinarily transmitted from man to man and hence does not occur in epidemic form. The rat flea, *X. cheopis* has been implicated in the transmission of scrub typhus, and ticks in other forms.

In spite of the fact that men sleeping on the ground, etc., were infected while officers and V.C.O.s who use cots escaped, there was some evidence that the disease was louse borne. The following facts may not be without importance. The epidemic was limited to one unit which proved to be louse infested, and within the unit, one company which was found to be free from lice was also free from the disease (except five men who were working with the infected companies). Moreover, there was a difference in the standard of personal cleanliness in the ranks, and prior to the outbreak during March there was an opportunity for lice to migrate from one to the other of the men's kits.

High agglutination results with OXK confirms that the epidemic was of 'K' form, but



Fig. 1.

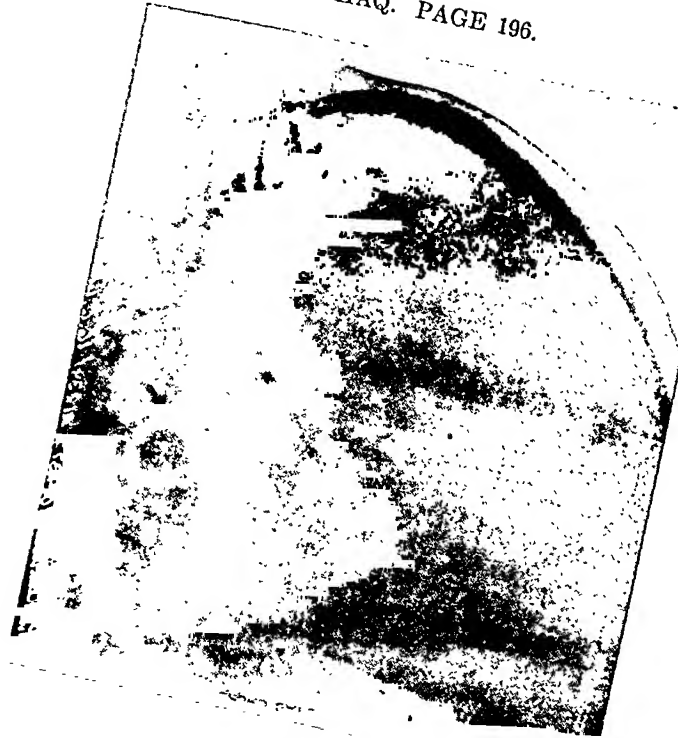


Fig. 2.

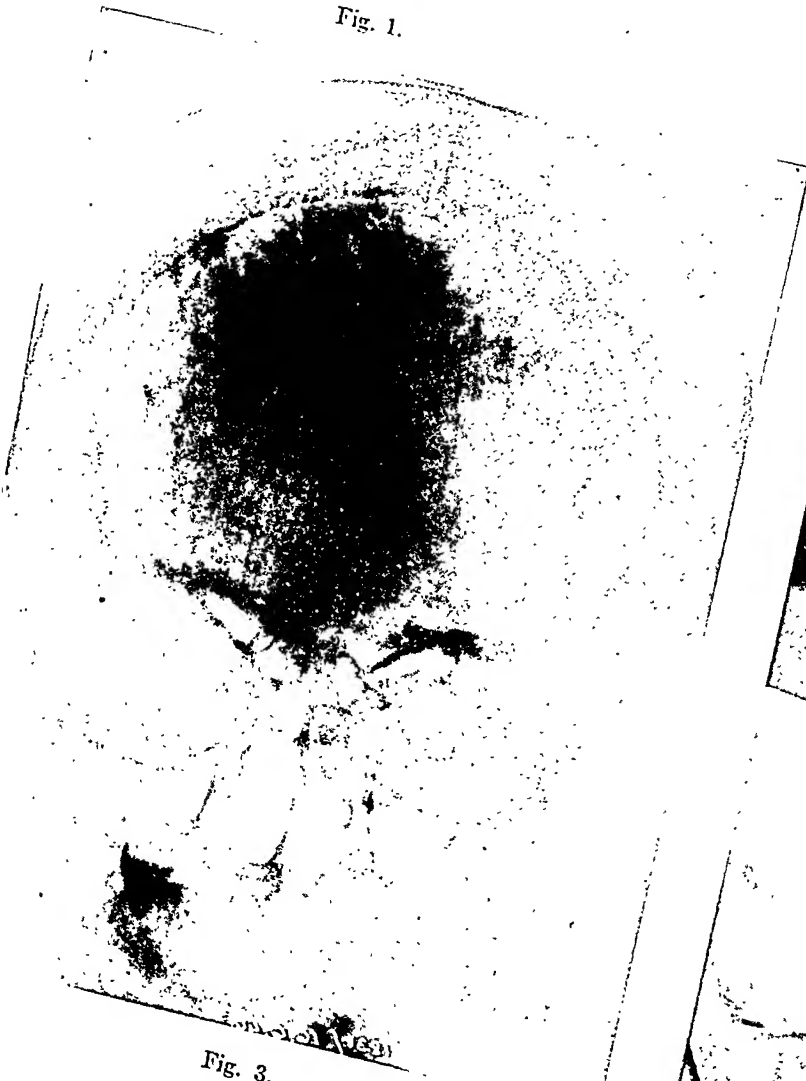


Fig. 3.



Fig. 4.

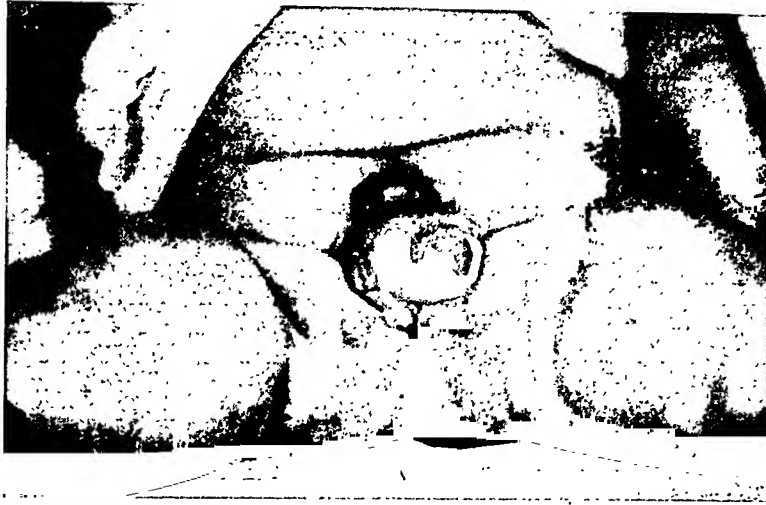


Fig. 1.—Photograph of a female child aged one year. Note the wide separation of the labiæ and the nipple-like projections of the ureters. The umbilicus is prominent with a small hernia.



Fig. 2.—Pycelogram showing the condition of the kidney. Note that the ureter is much bigger than normal. The minor calyces are cup shaped but not quite distinct. The pelvis is well defined and normal. The pubic arch is absent. At the ureteral opening, shadows of phalanges of two fingers are seen. They are two fingers pressing against the nipple-like projection of the ureteral opening to prevent the outflow of sodium iodide injected. In this case the clitoris was absent and could not be defined as such.

in about 16 cases there was an appreciable agglutination with OX19 and in 11 cases with OX2. This fact would appear to lend support to the view of Mooser, Varela and Pilz (1934) that the types and strains of typhus virus being so closely allied, their conversion into one another may be possible. The question whether a change of vector is likely to result in a change of strain also arises.

Conclusions

1. There is reason to suppose that in this outbreak of scrub typhus the disease, normally sporadic, achieved epidemic proportion owing to a change of vector, i.e. conveyance by lice within a louse-infested unit.

2. There is slight evidence that the disease was tending to change its strain, this being possibly associated with the change of vector.

3. In view of the epidemiological consequences of the above factors and the possibility of the relatively mild OXK type changing into the very fatal OX19 the following measures are recommended:—

(a) A careful watch for lice amongst the troops and effective disinfection wherever found.

(b) Disinfection of all admissions to hospital and their clothing.

(c) A careful watch for suspected typhus cases and rapid notification. Early diagnosis in the absence of rash and bite eschar is difficult.

(d) Full precautions (as for epidemic typhus) to be taken in the nursing of all typhus or suspected typhus cases.

[Note.—This paper raises some interesting and controversial points. It has long been known that scrub typhus could occur in large amount in local outbreaks. It is doubtful if it is necessary to explain this by postulating louse transmission.—Editor, I.M.G.]

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ECTOPIA VESICÆ

FOUR CASES

Pyelographic studies in a child aged one year

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EXTROPHY, ectopia vesicæ or extroversion of the bladder is an uncommon developmental defect of the bladder. In fifty thousand births, one foetus may suffer from this defect (Herman, 1938).

It is stated that this condition is due to the lack of junction of primary or extra-embryonic mesoderm arising between the amniotic and shield ectoderm behind the primitive streak and cloacal membrane and the secondary or intra-embryonic mesoderm derived from the primitive streak. This secondary mesoderm gives rise to the genital tubercle, the symphysis pubis, the intra-umbilical portion of the linea alba, and part of the mesoderm of anterior wall of cloaca. A defective development of secondary mesoderm from the primitive streak results in a considerable enlargement of the area of junction between the ectoderm and the endoderm around the cloacal membrane. The nutrition becomes poor as a result of this lack of contact, and probably this is the reason for the breaking down of the wall exposing the posterior and lateral walls of the cloaca on the anterior abdominal wall. The associated deformities of defective development of the symphysis pubis and genital tubercle, causing epispadias and split clitoris or hypoplastic organs, can thus be easily explained.

The prognosis of this condition depends upon the associated developmental defects, and is in some cases not incompatible with long life.

Keith (1908) has classified this defect in three groups, of which the third is definitely incompatible with long life. The individuals who live long often show the mental results of social and sexual isolation.

Thus there are complicated and uncomplicated types of ectopia vesicæ. The uncomplicated types are the most common, and usually are associated with a separation of the pubic bones and with epispadias in males. In these cases, usually the lower and mid portion of the abdominal wall is absent, and, through this, the bulging extroverted remains of the bladder with the ureteral openings are seen. In males, the penis in these cases will be rudimentary and usually epispadiac. In females, the clitoris will be bifid and hypoplastic or absent, the labiæ will be widely separated anteriorly, and if the clitoris is present the urethra will be epispadiac. The bladder mucous membrane, when it is exposed to the air, undergoes a change of keratinization, and becomes like skin, except at the ureteral openings where there is a semblance of the normal mucous membrane of the bladder. It becomes slightly œdematous, and forms papillary projections, hiding the ureteral orifices. In some cases as in the present instance (figure 1, plate VII) they appear like nipples, while in others they become retracted and overhung by these papillary projections of the mucous membrane. Associated with this, there is sometimes a defect in the umbilicus. When the umbilicus is present, there is a hernia as in the present case; sometimes the umbilicus is absent.

Four cases of extroversion of the bladder were seen by the author. The ages of the patients were 1 year, 3 years, 12 years and 14

years. Of the 4 cases, 3 were in males and 1 in a female child aged one year; this latter case is the one here reported. The umbilicus in this case was quite prominent, with a small hernia.

In this case, the opportunity was taken to make an attempt to find out if there was any other defect of the genito-urinary system, and also to ascertain the capacity of the pelvis of the kidney in a child aged one year. No previous record of this capacity was traced. The opportunity was taken to define the kidneys of the child. As the child was refractory and had to be kept quiet during the time of the ureteral catheterization, injection and x-ray, the child was anaesthetized. A careful watch over the pulse was kept at the time of injection of sodium iodide while doing the retrograde pyelography. When 2.5 c.cm. was injected, the child's pulse rate went up slightly, the injection was stopped; an x-ray was taken which gave a clear definition of the pelvis and calyces of the kidney (figure 2, plate VII). It is thus presumed that the normal capacity of the pelvis of a kidney in a child aged one year is between 2 and 2.5 c.cm.

The treatment of extroversion of the bladder is a great problem, and should not be undertaken in early life. Two cases were treated by transplantation of the ureters with the modifications suggested by Coffey and Wade. One of the cases was followed up for two years. The function of the kidney was also estimated by injecting uroselectan-B. It was found in this case that though the kidneys were secreting properly, the right side showed hydro-ureter and slight hydro-nephrosis. It was impossible to follow this case further. The second case was not traced after operation, and it is not known whether this operation has benefited him. He was a professional beggar.

In the third case, the child was aged one year, and though operation should not be undertaken at this age, the parents of the child insisted on operative interference in spite of the surgical risks. Even though the risk of the operation was pointed out to them, they were prepared to undergo the risk. A transplantation of the ureters was done. The child stood the operation well but died on the fourth day, having developed lung complications. The child had passed urine per rectum from the morning of the day after the operation.

Summary

1. Four cases of ectopia vesicæ are described of which three were operated on. Three were in boys aged 12, 14 and 3 and the fourth was in a female child aged one year.

2. The follow-up result of the functional aspect of the condition of the kidneys and the ureters is described after two years in one case.

3. The capacity of the pelvis in a child aged one year is assessed by a retrograde pyelogram as between 2 and 2.5 c.cm.

4. This case is reported especially with regard to the appearance of the pyelogram and the capacity of the pelvis of the kidney in a child aged one year.

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MODIFIED KLIGLER'S IRON AGAR MEDIUM FOR THE ISOLATION OF INTESTINAL PATHOGENS

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IN America, Kligler's iron agar medium is being largely used for the differentiation of intestinal pathogens from primary plate cultures of stools. The formula of the medium is as follows:—

Bacto-tryptone	20	gm.
Bacto-lactose	10	"
Bacto-dextrose	1	"
Sodium chloride	5	"
Ferric ammonium citrate	0.5	"
Sodium thiosulphate	0.5	"
Bacto-agar	15	"
Bacto-phenol red	0.025	"

Suspend the above 52 gm. in 1 litre of cold distilled water. Boil for 2 minutes to dissolve. Dispense in tubes and sterilize by autoclaving for 20 minutes at 15 lb. pressure (121°C.). pH after sterilization is 7.4±. Ferric ammonium citrate and sodium thiosulphate are hydrogen sulphide indicators and give clear-cut reactions. Best reactions are obtained in freshly-made media.

The medium is slanted in such a way that a generous butt end is formed, leaving a sloped surface at the top. Inoculation is done with putting a straight stiff wire deep into the butt end and then withdrawing it making a stroke on the sloped surface. Incomplete oxidation takes place in the butt end, and therefore acids generally form there turning the medium yellow-coloured. Red slant and yellow butt indicate fermentation of dextrose by dysentery and salmonella groups of organisms; yellow slant and yellow butt indicate fermentation of lactose by coliform organisms; absence of any change means non-lactose and non-glucose fermentation by alcaligenes, etc. We have found that dysentery organisms and vibrios either turn the slope alkaline, i.e. red-coloured, or leave this unchanged in colour and turn the butt end acid, i.e. yellow, the acid reaction

being feeble in the case of true cholera vibrios but marked in the case of non-agglutinating vibrios. *Bact. sonnei*, though a late lactose fermenter, behaves as above. With the salmonella group, including the typhoid bacillus, the butt end is acid and black at the junction and the slope is red. Some strains of *Bact. paratyphosum* A, *Bact. sendai* and *Bact. senftenberg* var. *Newcastle* do not give rise to a black colour, as these do not form H_2S . It was found that lactose non-fermenters such as *Bact. pseudocarinum*, *Bact. asiaticum* and *pseudoasiaticum*, *Bact. carolinum*, *Bact. diffuens* and *Proteus* gave rise to the same kind of reaction, i.e. alkaline or unchanged slope and acid butt like the dysentery organisms in addition to the formation of gas sometimes. Moreover, some pure cultures of coliform organisms gave reactions almost similar as above. Hence the specificity of such reactions in dysentery and salmonella group of organisms is doubtful. But it must be said that in the majority of the positive tests, the organism falls either to the dysentery or vibrio or salmonella groups of organisms. With all the strains of *Pseudomonas pyocyanea* and *Bact. faecalis alcaligenes* both ends were unchanged or slightly red.

We modified the standard Kligler's iron agar medium by replacing Bacto-tryptone with papain-digest meat broth, organic matter in the broth being adjusted to 0.75 per cent and other Bacto constituents as shown below. The modification was necessitated by the fact that 'Bacto products' were not available.

Papain-digest meat broth (organic matter 0.75 per cent)	100 c.cm.
Lactose	1 gm.
Glucose	0.1 "
Sodium chloride	0.5 "
Sodium thiosulphate	0.05 "
Ferric ammonium citrate	0.05 "
China grass	1.5 "
Phenol red, 1 per cent solution	0.25 c.cm.

pH is adjusted to 7.4 before adding phenol red. The medium is poured into tubes and autoclaved for 20 minutes at 15 lb. pressure (121°C.). It is needless to say that genuine ingredients were used.

The reactions generally obtained are represented in table I.

TABLE I

	Slant	Butt	H_2S
Lactose fermenters ..	Y	Y or Y + G	—
Salmonella group ..	R	Y or Y + G	+ or —
Dysentery group ..	R	Y	—
Vibrios ..	R	Y	—
<i>Proteus vulgaris</i> ..	R	Y G	±
<i>Bact. alcaligenes</i> ..	R	R	—
<i>Ps. pyocyanea</i> ..	R	R	—
Morgan's bacillus ..	R	R	—
<i>Bact. pseudocarinum</i> , <i>diffuens</i> , <i>asiaticum</i> , <i>carolinum</i> .	R	Y G	±

Y = yellow; R = red; G = gas.

The utility of Kligler's iron agar consists mainly in putting a suspected lactose non-fermenter into either a dysentery group or salmonella group. When it falls into one of these groups, it must be further tested by sugar and agglutination reactions. One advantage is that dysentery and salmonella groups of organisms are not missed by this test, and when Kligler's iron agar identifies it, slide agglutination from the culture on the slope of the medium can be done with polyvalent dysentery and salmonella sera. When slide agglutination is negative with either of the polyvalent sera, further tests, such as sugar reactions, motility, etc., need not be done unless it is necessary to put a specific name to the organism. If instead of the above medium, inoculation is made into liquid lactose medium which is much cheaper than the above medium, more saving is achieved only when lactose is fermented, but when lactose is not fermented, an agar subculture must be made and then slide agglutination done. When lactose is not fermented such a procedure of putting into liquid lactose becomes more expensive, and more time is needed to get a preliminary report ready. It is for these reasons that Kligler's iron agar is considered to be an advantage in isolation and identification of intestinal pathogens.

The following procedure was adopted in the use of modified Kligler's iron agar (table II).

1. The medium was used fresh as far as possible. If the medium was not used soon

TABLE II

Slant	Butt	H_2S	Gas	Abbreviation used	Indication	Diagnosis
Red	Yellow	—	—	Alk	Fermentation of dextrose	Shigella Vibrios.
Red	Yellow	±	±	Alk B G	Fermentation of dextrose	Salmonella.
Yellow	Yellow	—	+	A ± G	Fermentation of lactose	Coli-aerogenes group.
Red	Red	—	—	A + Alk Alk	No fermentation of lactose and dextrose.	<i>Ps. pyocyanea</i> , <i>Bact. faecalis alcaligenes</i> .

Yellow = acid; red = no change or alkaline; black at the junction = H_2S . $\frac{Alk}{A}$ = $\frac{\text{alkaline slant}}{\text{acid butt}}$; B = blackening; G = gas; + = positive; ± or ± = sometimes positive, sometimes negative.

after preparation, it was preserved in the ice-chest in test tubes without making slopes and was melted and sloped afresh before use.

2. When used, the butt end was first stabbed with a straight stiff wire charged with the material and a linear stroke was made on the slant afterwards.

3. The result was read after 18 to 20 hours' incubation.

4. Slide agglutination of cultures from slopes with polyvalent dysentery and salmonella sera was done.

(a) If the slide test was positive, common monovalent sera were used and for corroboration sugar tests and, if necessary, agglutination by Dreyer's method were done.

(b) If the slide test was negative, but the reaction highly suggestive of a lactose non-fermenter, sugar tests were done to identify the organism.

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THE USE OF BLOOD TESTS IN EXCLUDING PATERNITY AND MATERNITY

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THIS communication is an amplification of a previous communication by the writer (Grevall, 1939) and is published in response to several enquiries received last year.

Disputes in paternity and maternity arise: (1) When a child is alleged to be supposititious. This appears to be the commonest cause in India. (2) When a man is averred by a woman to be the father of her child. This is the commonest cause in Europe. (3) When a husband avers that he is not the father of his wife's child. (4) When children are suspected to have been changed in a maternity hospital.

INHERITANCE OF BLOOD CHARACTERS

The attached tables of inheritance of three sets of characters, (i) O, A and B, (ii) M and N, and (iii) Rh+ and Rh- will indicate whether

or not it is possible for a child to be the offspring of a certain parent, or conversely, whether or not it is possible for a parent to be the father or mother of a certain child.

From table I two laws emerge: (1) Characters A and B cannot appear in the offspring unless they are present in one or both parents. This limitation does not apply to the character O which is *recessive* while A and B are *dominant*. A parent of group A in *phenotype* (as found by serological test) may be either AA or AO in *genotype* (as constituted by fertilization of the ovum, each parent contributing his or her character-carrying *gene* on the chromosome, the dominant character only manifesting itself). When two parents of genotypes AO and AO come together, an offspring of the genotype OO is possible. The same reason applies to the phenotype B which may be in genotype BB or BO. AO and BO will also supply an OO combination. (2) A parent O cannot have an offspring AB nor can a parent AB have an offspring O. O is genotypically OO and one of the two genes must unite with O, A, or B from the other parent, yielding OO (=O), OA (=A) and OB (=B): the combination AB is not available. Similarly, AB is genotypically composed of A and B and one of the two genes must unite with O, A or B from the other parent: the combination OO (yielding O) is not available.

A₁ is dominant over A₂ which is dominant over A₃. The subgroups of A, however, are ignored by many for forensic purposes, because of difficulties in the technique.

From table II also two laws emerge: (1) M and N cannot appear in the offspring unless they are present in one or both parents. (2) A parent M cannot have an offspring N nor can a parent N have an offspring M. The genetic basis of the inheritance is the fact that both M and N are dominant. The genotypes of the phenotypes M and N being MM and NN respectively, M from one parent cannot be suppressed by N from the other parent, nor can N be suppressed by opposite circumstances.

Table III is shown in its early and simple form. Two rules emerge: (1) Rh- couples cannot have Rh+ offspring. (2) Rh+ and mixed couples can have Rh+ and Rh- offspring. The explanation of this simple scheme is that the Rh+ character is carried by the dominant gene Rh and the Rh- character by the recessive gene rh. The genotype of the phenotype Rh+ may be (i) RhRh or (ii) Rhrh, while the genotype of the phenotype Rh- can only be rhrh. The second of the first two genotypes mating with a similar genotype (Rhrh- Rhrh) or with an rhrh genotype (Rhrh rhrh) can provide three combinations (RhRh, Rhrh, rhrh), while the genotype rhrh mating with a similar genotype (rhrh rhrh) can only provide one (rhrh).

The study of the hæm(agglutin)ogen Rh has advanced so rapidly during the last two

years that now there are no less than six genes: Rh, Rh₁, Rh₂, Rh', Rh'' and rh (Wiener, 1944). Besides, anti-rh sera (anti-Hr and St. sera) have been described (McColl, Race and Taylor, 1944) which do not fit into the scheme of dominance and recessiveness (Greval, 1944). Recently yet another gene Rh_y has been added (Race and Taylor, 1944). Probably the situation will be modified when it is more critically examined and overlapping eliminated. It cannot be considered static enough for forensic purposes, at present.

SEQUENCE OF TESTS

A and B are determined first. If they fail to exclude the relationship M and N are tried next. In future, the Rh+/- states will also be utilized. The sequence is a matter of convenience, not indicative of any interdependence between the three systems of blood characters.

NEGATIVE AND POSITIVE FINDINGS

The negative finding is definite while the positive finding indicates a possibility only. It can be stated definitely that Master Tom is *not* the son of Mr. Smith. It cannot be stated equally definitely that he is the son of Mr. Brown. That he *can* be the son of Mr. Brown is all that can be stated on the positive side. The same remarks apply to Mrs. Smith and Mrs. Brown regarding motherhood.

PARENTAGE EXCLUDED BY THE EXAMINATION OF ONE PARENT ONLY

This is possible when the second law of inheritance of blood groups and blood types applies. A parent O cannot have an offspring AB, no matter what the group of the other parent is: nor can a parent AB have an offspring O, no matter what the group of the other parent is. Similarly, a parent M cannot have an offspring N, no matter what the type of the other parent is: nor can a parent N have an offspring M, no matter what the type of the other parent is.

MORE EVEN DISTRIBUTION OF BLOOD GROUPS IN INDIA THAN IN EUROPE AND AMERICA

The various blood characters have a distinctive distribution all over the world. The following percentages are given for comparison:—

	O	A	B	AB
Indians, Calcutta	35.03	22.5	34.9	7.9
English, London	45.9	42.0	9.3	2.7
	M	MN	N	
Indians, Calcutta	42.7	46.7	10.7	
English	32.5	48.5	19.5	
	Rh +	Rh -		
Indians, Calcutta	90.0	10.0		
White Americans	85.0	15.0		

The fact that O, A, B and AB are more evenly distributed in India than in Europe and America, and *therefore give more information*, has not yet been fully realized.

DIRECTIONS FOR GETTING BLOOD TESTED

When fresh blood can be given

The persons concerned visit a serological laboratory with their photographs. The serologist will test the blood and issue the report, keeping his record in the usual register as well as on the photographs.

When blood is sent to a distant laboratory

The writer's laboratory requires the following: (1) About 0.25 c.cm. of blood dried as a stain on chemically pure filter paper, not in the sun. An unstained part of the filter paper should also be available as a control. (2) About 0.5 c.cm. of clear serum in an ampoule. This is taken from a test tube in which about 3 c.cm. of blood have been put and allowed to clot *under sterile conditions*, without disturbing the tube. (3) About 0.5 c.cm. of serum turbid with rbc in an ampoule. This is taken after shaking gently the contents of the tube, after the clear serum has been removed. The specimens are taken by a responsible medical man (preferably an official) and sent in a sealed and registered parcel. The impression of the seal is sent in another registered parcel.

The group is determined from the stain by absorption. The serum corroborates the finding. The rbc preserved in the turbid serum (if all has gone well with sterility) also corroborate the findings. If the groups exclude the parentage a report stating the facts and conclusions is issued. If the groups do not exclude the parentage determination of types is suggested. For this purpose fresh blood is required.

Opinion is withheld if a 'defective group' [in which an iso(haemagglutinin) which could be present is absent] or an anomalous reaction complicates an incompatible combination of groups (not in accordance with the tables). Fresh blood is required for repeating the tests.

JUDICIAL ASSESSMENT OF THE EVIDENCE ON BLOOD GROUPS AND BLOOD TYPES

The courts keep the evidence of blood groups and blood types on the same footing as any other evidence (an Editorial, 1944).

(Greval and Chandra, 1940)
(Taylor and Ikin, 1939)

(Greval, Chandra and Woodhead, 1939)
(Harley, 1936)

(Greval and Chowdhury, 1943)
(Landsteiner and Wiener, 1940)

The sequence of relevant events is as follows: (1) In 1938 a case was decided in England on the evidence of blood types (an Editorial, 1938). (2) In 1939 a provision was made for the evidence of blood tests in the Bastardy (Blood Tests) Bill introduced in the House of Lords by Lord Merthyr (an Editorial, 1939). (3) In 1941 a case was decided in India (Charlewood, 1941) on the evidence of blood groups. (4) In 1944 the evidence of blood types was not considered reliable in a case in England (an Editorial, 1944). The judge 'did not, having heard and seen the wife, think she was of a type that commits adultery'.

Commenting on the last event the expert writing the editorial referred to above observes with satisfaction: 'Few who heard the decision doubted its wisdom. It would be an evil day for our courts if they ever felt obliged to elevate scientific evidence into a class by itself, instead of, as at present, keeping it on the same footing as other evidence.'

Commenting on similar events in general, another expert complains: 'In uncontested divorce actions, an exclusion of paternity by the blood tests is usually accepted without question by the court, but when the action is contested, unfortunately, there are still some judges who believe the obviously false testimony of the mother even though the objective findings of the blood tests prove that the husband is not the father of the child in question' (Wiener, 1944).

Evidently there exists on this point a difference of opinion between experts, which needs explanation, although the authority of the court is undeniable.

A danger of inverting the evidential value of the blood tests also exists under the circumstances complained of. The negative finding that Master Tom *cannot be* the son of Mr. Smith, which is fully guaranteed by the known laws of genetics, is likely to be ignored if the mother's looks and voice impress the judge in her favour. On the other hand, a positive finding of the possibility only, that Master Tom *can be* the son of Mr. Brown, is likely to be unduly stressed by the defence or even by the impressed judge.

SUMMARY

1. The commonest cause of disputes in paternity and maternity, in India, is the supposititious child.

2. Inheritance of blood characters has been tabulated and explained genetically.

3. In the tests for excluding parentage, group is determined first and the type later. The Rh+/- state cannot yet be utilized.

4. Negative findings are conclusive while positive findings only indicate possibilities.

5. Under certain conditions the parentage can be excluded by examining the child and one parent only.

6. Blood groups in India are more evenly distributed than in Europe and America, and therefore give more information.

7. Directions for getting bloods tested, by attending personally or by sending specimens by post are given.

8. Evidential value of the blood tests in courts is the same as that of any other evidence. It is not elevated into a class by itself as a definite scientific finding. On this assessment of the evidence experts do not agree.

TABLE I

Blood groups in parents and children

	Parents	Children possible	Children impossible
1	O × O	O	A, B, AB
2	O × A	O, A	B, AB
3	O × B	O, B	A, AB
4	A × A	O, A	B, AB
5	A × B	O, A, B, AB	..
6	B × B	O, B	A, AB
7	O × AB	A, B	O, AB
8	A × AB	A, B, AB	O
9	B × AB	A, B, AB	O
10	AB × AB	A, B, AB	O

TABLE II

Blood types in parents and children

	Parents	Children possible	Children impossible
1	M × M	M MN N
2	M × MN	M MN ..	M .. N
3	M × N	.. MN ..	M .. N
4	MN × MN	M MN N
5	MN × N	.. MN N	M
6	N × N N	M MN ..

TABLE III (Provisional)

Rh+/- states in parents and children

	Parents	Children possible	Children impossible
1	Rh+ × Rh+	Rh+, Rh-	..
2	Rh+ × Rh-	Rh+, Rh-	..
3	Rh- × Rh-	Rh-	Rh+

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SULPHATHIAZOLE AND ACUTE MASTOIDITIS

By A. G. CHACKO, B.A., M.B., B.S.

ACUTE mastoiditis is a condition for which we advocate immediate operation by a specialist in a well-equipped hospital. The general practitioner is often quite incompetent to deal with this complication. The anatomy of the temporal bone will have to be carefully studied, and considerable experience is necessary before we can attempt an operation on this region. The facial nerve in its course round the middle ear, will have to be carefully preserved. Any injury to the labyrinth will be a tragedy. No wonder very few doctors attempt to do a mastoid operation.

The efficacy of the sulphonamide group of drugs in cases of acute otitis media is very striking. Under local treatment, these discharging ears often necessitated long treatment. Ear drops have only a limited value in this condition. Now, the administration of the sulphonamides, preferably sulphathiazole for a few days with or without ear drops, is often followed by a dramatic cure in a large number of cases. This led me to try sulphathiazole in several cases of acute mastoiditis with quite astonishing results. A few case reports will illustrate this:—

1. A girl, aged 5 years, was brought to me with a fluctuating swelling behind the ear over the mastoid region, accompanied by fever. There was a history of discharge from the ear which suddenly stopped, followed later by this swelling. The diagnosis was obvious, and I advised immediate operation which the relatives refused. I gave her sulphathiazole tablets three per day for 3 days, and the swelling completely disappeared. The child is quite fit even now, and there is no discharge from the ear and absolutely no deafness.

2. A lady, about 35, was brought to me about a month back, with acute pain in the ear. She had been running from one doctor to another with apparently no relief; possibly

all doctors advised operation which she refused. On examination, there was profuse discharge from the ear with very marked mastoid tenderness. She had had severe headache and no sleep for four days; there were a furred tongue, and all the indications for immediate operation. I decided to try sulphathiazole, the usual dose, and she had a comfortable night, the first one for many days. She was completely cured after three days of intensive therapy, with no recurrence so far.

3. Another child, 3 years old, was brought with a history of discharge from the ear and a well-marked fluctuating swelling over the mastoid region. There was a sinking in of the posterior upper region of the external meatus, and the child was in acute distress. As there was a large quantity of pus just beneath the skin of the mastoid region, I incised the abscess at the most prominent area and gave her sulphathiazole, 3 tablets a day, for 4 days. Recovery was rapid.

There is no doubt regarding the usefulness of the Schwartz operation in chronic cases of mastoiditis. This note is written to point out the efficacy of sulphathiazole in acute mastoiditis especially for those doctors practising in upcountry places and also for those patients who cannot or will not go to a specialist for operation. An intensive therapy for 3 or 4 days is quite sufficient to determine whether sulphathiazole is effective in a particular case. It is quite unlikely that any infection of the brain or meninges might take place during this interval, as the patient is under the influence of one of the most potent anti-bacterial drugs.

Acute mastoiditis is more likely to affect the cellular type of mastoid and this being more vascular, sulphathiazole acting through the blood stream, can cure this condition. Perhaps the Schwartz operation or the radical mastoid operation may be relegated to cases of chronic mastoiditis where the bone is acellular. Penicillin may be better in acute mastoiditis but it is not available in sufficient quantities at present for an extensive trial.

TYPHUS FEVER IN GILGIT

By D. S. JACKSON

MAJOR, I.M.D.

THE last paragraph in the Editorial of the *Indian Medical Gazette* for April 1944, to the effect that most of the recorded cases of typhus in India have been in the Army, has induced me to send in these notes on typhus fever as seen in this district.*

In the last nine months, I have seen and treated personally 213 cases, and I would like to record my impressions. These notes

*This remark was made of endemic typhus in the plains of India. Epidemic typhus is of course not uncommon in hill people—EDITOR.

only apply to those treated in hospital. Sporadic cases started occurring in Gilgit district early in 1943, but did not assume epidemic proportions till December. The seasonal incidence of the 213 cases is shown below :—

Months	Average day temperature	Number of cases. Admissions	Deaths
November ..	46°-57°	6	..
December ..	41°-66°	11	..
January ..	41°-50°	12	..
February ..	39°-60°	17	..
March ..	60°-72°	40	2
April ..	54°-89°	29	..
May ..	61°-99°	38	1
June ..	64°-102°	32	1
July ..	85°-112°	14	1
August ..	73°-104°	4	..
		213	5

Mortality : 2.4 per cent.

I presume that this is an epidemic outbreak of louse-borne typhus, but nothing is known for certain about the mode of infection. It may possibly be tick typhus as described by Megaw in 1917, or possibly flea typhus which is reported to occur in the Simla Hills, but I am convinced that the louse is the culprit.

Most of the cases occurred among the poor classes, the only well-to-do people who were attacked being among the hospital staff. The doctor in charge of the medical ward, a compounder, and the clerk dealing with medical ward files all had severe attacks of the disease.

Clinical manifestations were surprisingly alike in all the cases. Prodromata such as lassitude, headache, etc., as described in the textbooks, were conspicuous by their absence, the onset was always sudden with a rapid rise of temperature, rigor, severe headache, vomiting, general pains and a flushed face. Prostration was rapid and the patient looked dazed and semi-comatose by the 3rd day.

Delirium was a very common symptom and occurred in about 80 per cent of the cases, starting on about the 5th to the 7th day, coinciding with the advent of the rash, and lasting till the temperature began to fall.

Rash.—There was a well-marked rash in every case without exception. In the series of 41 cases reported in the *Indian Medical Gazette* of April 1944, the rash was conspicuous by its absence. In my series, the rash was typical and did not vary in type. It appeared from the 5th to the 7th day on the axilla, chest and abdomen, gradually spreading to the back and limbs. It took the form of sub-cuticular mottling later turning dull pink, and then becoming petechial in spots, looking exactly like flea bites. These generally faded

by the 12th to the 14th day, though sometimes a brown staining persisted for as long as three weeks from the onset of the disease.

The temperature in most cases came down by lysis, reaching normal on about the 14th day.

There was no marked abdominal distension or tenderness. The spleen normally showed no enlargement. No serological tests were done, as laboratory facilities are not available. A blood film was always taken to exclude malaria.

Complications.—The only complications of any note that occurred were pneumonia, usually lobar in type and suppurative parotitis. Each of these complications occurred in about 5 per cent of the cases.

Treatment was mainly symptomatic with careful nursing. It was not possible to use intramuscular injections of convalescent serum, as there was none available. It was found that a salicylate mixture was very useful.

Luminal 2 gr. daily, repeated if necessary, was found helpful in controlling delirium.

Chemotherapy with the sulphonamide group of drugs has no place in the treatment of typhus. It is conceivable as in typhoid fever, they may depress the body resistance and cause agranulocytosis. Cases complicated with pneumonia were however treated with M&B 693.

Quinine appears to be a harmful drug in typhus. Two patients, given intramuscular quinine injections, did very badly and died.

All patients were given frequent Condy's fluid gargles, and the mouth was kept scrupulously clean.

Diagnosis.—Diagnosis was very easy in most cases, the typical rash making it difficult to mistake it for anything else. The people in these northern climes are comparatively fair-skinned, making it easy for the eruption to be seen. I am sure that any of my compounders can recognize a typhus rash on sight.

I have said nothing new or startling in these notes. The points that struck me about this epidemic were the low mortality, and the similarity of the symptoms in every case, making diagnosis easy.

The hospital staff and government employees were given three injections of typhus vaccine (Cox type) at intervals of one week. So far, only one protected person has had typhus, and that a very mild attack.

Attempts have been made to educate the public in cleanliness, and I have had circulars issued to villages, and public announcements pointing out that the best way to combat the disease is by absolute personal cleanliness, not only by bathing and washing clothes frequently, but also by keeping houses as clean as possible, and most important of all, by placing their bedding in the sun daily.

I must thank the Political Agent, Gilgit Agency, for permission to publish these notes on typhus in the Agency.

FAMINE ŒDEMA AND ITS TREATMENT WITH MERCURIAL DIURETICS

By JOHN LOWE, M.D. (Birmingham)

and

H. CHAKRAVARTY, M.B.

(From the School of Tropical Medicine, Calcutta)

IN the Bengal famine of 1943-44 in the affected population and among the patients in the hospitals and camps for sick destitutes occurred many cases of generalized œdema, and among these patients many deaths occurred, the terminal event usually being œdema of the lungs.

In some of these patients, the œdema was caused by some definite disease present, for example severe anæmia, chronic malaria, severe hookworm infection, advanced kala-azar, etc., and a few definite cases of acute nephritis were encountered. In many of the cases, however, the condition was apparently nutritional in origin and corresponded closely to what has been described in the literature of famine as famine œdema. It is not the object of the present note to discuss in detail the nature, ætiology, signs and symptoms of this condition, since we are concerned here mainly with treatment, but we will give a brief outline of the clinical picture.

The condition may be seen at any age and in either sex with prolonged semi-starvation and exposure, possibly complicated by attacks of malaria, dysentery or diarrhœa. Œdema of the subcutaneous tissue begins to appear. It always appears first in the most dependent parts, the feet and legs, and it may spread to the arms and hands, to the abdomen with the occurrence of marked ascites. Œdema of the genital organs is frequently marked. Œdema of the face is slight or absent except at a late stage. This differentiates it markedly from the œdema of nephritis, and also, of course, the absence of the characteristic changes in the urine.

Ascites is often a marked feature, and this seems to be accentuated by the occurrence in many of the patients of enlargement of the liver with some evidence of cirrhosis and portal obstruction. This condition of the liver seen in famine cases cannot be discussed here. It has been a very striking feature in many cases, and tends to support the recently-developing idea that a dietetic or nutritional factor may be concerned in the causation of cirrhosis. With the development of marked ascites, fluid is found in the pleural cavities and there then develops œdema of the lungs which is often a terminal event.

The effect of posture on the distribution of œdema is marked; the fluid shifts according to which side the patient lies on.

In these cases, the absence of enlargement of the heart and the absence of tachycardia and

also of any evidence of peripheral neuritis differentiate the condition clearly from the 'wet' form of beriberi.

Hypoproteinæmia has been a common finding, but in some cases this has been slight, and the chief change was not in the total plasma protein but in the albumin-globulin ratio. Total protein as low as 3.5 grammes per cent has, however, been recorded. Anæmia is usually present, but it is not of such a severe degree as to explain the œdema. Owing to the massive œdema present, the emaciation of the patient may be completely masked, although the thinness of the face contrasts markedly with the swelling of the dependent parts of the body.

A feature in that of many of these cases has been the history of recurring attacks of diarrhœa. During an attack of diarrhœa, the œdema diminishes, and when the diarrhœa ceases, or is controlled by treatment, the œdema increases, but weakness is progressive throughout. These attacks of diarrhœa differed rather markedly from the nutritional diarrhœa described by Aykroyd and Gopalan (1945), but this matter cannot be discussed further here.

We would, however, note that, although it was unusual to isolate any pathogenic organism in these cases of diarrhœa, the diarrhœa often responded excellently to the administration of drugs of the sulpha group, particularly sulphaguanidine or sulphathiazole. As stated above, however, the control of the diarrhœa in this way was frequently followed by an increase in the œdema.

In cases of famine œdema, the urine output is persistently low, a trace of albumin is frequently present, but definite evidence of nephritis in the form of red blood cells, casts, granular or even hyaline, is absent.

The blood pressure seen in these cases varies rather considerably. During and after attacks of diarrhœa, the blood pressure is frequently low, sometimes very low, but in the presence of a generalized œdema the blood pressure is often normal, and may even be slightly on the high side. It appears to us that the patients with a high blood pressure responded better to the treatment mentioned below.

Treatment of the condition.—The rational form of treatment of the condition appears to be by diet, preferably a high protein diet, to remedy hypoproteinæmia which appears to underlie the condition. In less marked cases, all that is needed is rest and good diet; and with this treatment the œdema in some cases will disappear within a few days, although it tends to recur when the patient gets about. In severe cases in our series control of the condition by hospitalization and diet has been difficult or impossible. The administration of a good diet rich in protein will frequently bring on profuse diarrhœa with rapid deterioration of the patient's condition although the œdema may get less.

Other forms of treatment suggested have been the intravenous injection of suitable protein solutions such as protein hydrolysate. This appears to have beneficial results in some cases, particularly those with low blood pressure, but the evidence of the value of protein administration is not conclusive. Moreover, in patients with general anasarca and oedema of the lungs, one hesitates to give large amounts of fluid intravenously.

A number of cases were treated with vitamins, multi-vitamin tablets, and also individual vitamins, particularly vitamin B₁. The response to this treatment was never marked, and often very slight or absent. Another form of treatment which might be beneficial is the giving of intravenous transfusions of blood serum, blood plasma reconstituted from dried serum, or dried plasma but in more concentrated form than usual, perhaps only half the usual amount of distilled water being added. So far, we have had no opportunity of trying this form of treatment which would seem to be, in many ways, ideal.

In this hospital, it was thought worth while to try the effect of mercurial diuretics in patients with general anasarca and oedema of the lungs. It was not expected that the treatment would have any permanent beneficial effect, but it was thought that it might tide the patient over the crisis when oedema of the lungs was present or threatened. The number of cases treated in this way in this hospital has not been very large, about 20, but in some cases the immediate results have been very striking, and moreover, to our surprise, the benefit in many of the cases seems to be permanent. It should be stated, moreover, that this treatment had been applied only to cases in which other modes of treatment had failed to produce any benefit.

The best way to indicate the type of results which have been seen in these cases is to quote some case reports.

Case 1.—A boy, aged 12, admitted from a famine orphanage with a report from the medical officer to state that he had been in the orphanage with good food and care for six months during which time he has had alternating attacks of diarrhoea and generalized oedema. Attempts to increase the diet caused a recurrence of diarrhoea; cutting down the diet reduced the diarrhoea but increased the oedema.

On admission, the patient was very emaciated and weak, was suffering from diarrhoea and had some oedema. The liver was large and hard and the veins on the abdominal wall were dilated. Some ascites was present; weight 34 pounds; serum protein 4.9 gm. per cent; albumin and globulin equal; blood pressure 70 and 50. Urine output was low, and the urine showed only a trace of albumin.

The diarrhoea was controlled by sulphaguanidine, but the oedema rapidly increased with an increase in body weight of 5 or 6 lb. in a few days. Accordingly the patient was given ammonium chloride by mouth and $\frac{1}{2}$ c.cm. of neptal (May & Baker) by injection. That day, 68 oz. urine were passed, and the oedema became less. Two days afterwards, the diarrhoea started again, and once more sulphaguanidine was given which controlled it, but the oedema, ascites, etc., returned. This

time $\frac{1}{2}$ c.cm. of neptal was given. The diuresis was not marked, only 40 oz., but from that time the urine output has continued at a reasonable level. Within a few days of these two injections of neptal, the oedema disappeared and also the ascites, and the general condition improved rapidly. It was found possible to increase his diet, and neither the diarrhoea nor the oedema recurred. After two months in hospital, his weight has increased by 22 lb. in spite of the disappearance of the oedema, the blood pressure rising to 90 and 60. The liver though still palpable is smaller. The plasma protein value is now 7.4 gm. per 100 c.cm., and the patient is about to be discharged practically normal. Some enlargement of the liver and dilatation of the veins on the abdominal wall are, however, detected.

Case 2.—Male, aged 30, with a history of prolonged semi-starvation, weakness and attacks of diarrhoea. The emaciated condition of the patient is hidden by a generalized oedema and ascites, the oedema being very marked in the dependent parts. The chest showed moist sounds, and the condition suggested some oedema of the lungs. Blood pressure was 130 and 90. Haemic murmurs in the heart; serum protein 6 gm. per cent, globulin 3.2, albumin 2.8. Urine output is low with a trace of albumin. Marked diarrhoea is present.

For several days after admission, the patient was given no special treatment except rest and diet. The diarrhoea and oedema persisted unchanged. The diarrhoea was treated with sulphaguanidine and was controlled, but the oedema persisted and increased. In the first two weeks in the hospital, his weight increased from 89 to 98 pounds owing to an increase in the oedema. He was then treated with ammonium chloride and salyrgan (Bayer). After the injection of $\frac{1}{2}$ c.cm. a diuresis of 80 oz. occurred, then the urine output fell again. Four days later, an injection of 1 c.cm. was followed by a diuresis of 100 oz. followed by a fall in the urine output. A week later, a third injection of 2 c.cm. produced less marked immediate diuresis, but the urine output from then on remained at a reasonable level. With this treatment, within 14 days the patient's weight came down from 98 and 74 lb. owing to the disappearance of the oedema. Then it was possible to increase his diet without producing diarrhoea. The patient was discharged from the hospital about a fortnight later, still weak and emaciated, but with no diarrhoea and no oedema.

Case 3.—Male, aged 30, with a history of semi-starvation and diarrhoea, showing a generalized oedema and marked ascites with moist sounds present in the chest. Blood pressure 105 and 80, urine output low, with a trace of albumin. Plasma protein 6.4 gm. per cent, globulin 4.1, albumin 2.3. The patient's emaciated condition was masked by the oedema. After 7 days' hospitalization and diet, no improvement was seen; his weight was reduced by only 2 lb. He was then put on neptal treatment, four injections being given during the next two weeks. During this time, his weight fell from 110 to 87 lb., a fall of 23 lb. After the fourth injection, the urine output remained good and his weight was further reduced a little. During the next few weeks, his diet was increased with an increase of several pounds in weight and no recurrence of diarrhoea, or oedema, and he was discharged in good general condition, plasma protein being 7.6 gm. per cent, albumin and globulin being equal, 3.8 gm. per cent.

The response in all cases of famine oedema was not equally good. As stated above, in patients with a low blood pressure and inanition, the response was often relatively poor, although if the general condition and the blood pressure improved the response also improved. In patients with serious infections, for example kala-azar and tuberculosis of the lungs, the response may be poor, and also in very severe

anæmias; even in kala-azar, however, this treatment has proved useful.

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A Mirror of Hospital Practice

A CASE OF HYPERGLYCÆMIA SHOWING AN UNUSUAL RESPONSE TO THYROID THERAPY*

By RANITA VETHAVANAM, M.B., B.S.,
M.R.C.P. (Lond.), etc.

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'Mrs. X, a doctor aged 42, was admitted to hospital on 29th March, 1943, for the treatment of hyperglycæmia. A few days previously, a Medical Board had rejected her as unfit for military service owing to the presence of sugar in the urine and palpable spleen and liver.

History. General.—The patient stated that she was thin and under-developed in early adult life and that while a medical student her age was taken to be fourteen; she was treated with thyroid. She had an abundant growth of thick hair while at college, but it had gradually fallen and become thinner in quality. Her skin always tended to be greasy. She married at the age of 30, and her weight increased gradually afterwards up to 11 stones 2 lbs. She had mild attacks of asthma in 1929 and several similar attacks up to 1939. She had rheumatic fever in 1937. She worked in Burma as a doctor until evacuated in May 1941.

Gynæcological.—Catamenia at 11½ years; periods regular and rather profuse; no conceptions. Menopause with high fever at 33 years following a plague inoculation. Treatment with multi-glandular pills with pituitary extract for early menopause produced severe headaches.

Family.—Her sisters were all thin like her and grew fat after childbirth. Two brothers suffer from urticaria.

Physical examination.—She was rather obese, weight 9 stones 6 lbs., height 5 feet 2 inches; alert and active; skin slightly coarse, and complexion blotchy; pulse 80; blood pressure 126/80; spleen not palpable; liver could not be palpated owing to a thick abdominal wall. Except for a prolonged expiration heard all over the chest, other systems were found normal.

Laboratory examination.—Blood examinations revealed no abnormality in the blood picture or in the counts. The blood cholesterol was 267 mgm. per cent. Eye examination showed no abnormality. Stool examination showed no ova or amœbæ.

A sugar tolerance curve done on 26th March, 1943, showed a fasting blood sugar of 394 mgm. and a maximum rise to 588 mgm. two hours after giving glucose; the patient was on extra high carbohydrate diet for two weeks before this. On the 3rd April, 1943, the fasting blood sugar was 428 mgm.

Treatment.—The patient was kept on a reduced diet of 1,517 calories for about a week, and as there was no improvement, thyroid ¼ grain twice daily for 12 days and 1 grain twice daily for 8 days was given and the diet was further reduced by about 200 calories. With this treatment, the weight came down by 3 lbs. and the fasting blood sugar from 428 to 160 mgm.; the B.M.R. rose from -13.6 to -9.4.

Thyroid was now stopped, but the same diet was continued for about three weeks. At the end of the first week the fasting blood sugar rose to 176 mgm. Thyroid was again started ½ grain twice daily, and the weight and fasting blood sugar came down within two weeks. Ordinary hospital diet of 2,311 calories was now resumed and thyroid continued; a week after this regime there was a rise in the fasting blood sugar. 'Panmelitus' 2 tablets twice daily was given for a week but the fasting blood sugar continued to rise. The diet was then reduced to 1,632 calories and insulin was given 40 units daily for 2 days and 8 units daily for another 2 days. There was no reduction in the fasting blood sugar.

The patient was discharged from hospital on 10th June, 1943, and advised to continue thyroid ½ grain twice daily for 3 months with a diet of roughly 1,600 calories and no carbohydrate restrictions. At the end of this period, her weight was 8 stones 11½ lbs. and the fasting blood sugar came down to 130 mgm. Thyroid was then stopped; 15 days later the weight was less by 2 lbs. but the fasting blood sugar rose to 137 mgm.

Urine examination throughout her stay in hospital and afterwards was negative for sugar except once when there was just a trace.

Discussion.—The interest in this case lies in: (1) The apparently symptomless high blood sugar levels and the high renal threshold. Though clinically the case was not a well-defined case of hypothyroidism the patient seemed to do well on thyroid. Her complexion and skin improved. She felt generally better and thought that her memory had improved; her former employer remarked that he had never seen her look fitter. This fact along with her history of under-development in adolescence, sterility, and early menopause, and the tendency to obesity, suggests that this is a case of hyperglycæmia due to endocrinal imbalance, not falling within any of the recognized types.

(2) The hyperglycæmia failed to respond to diet alone. The fasting blood sugar on 3rd April, 1943, was 428 whereas with thyroid therapy

*Paper condensed by editor.

and with a slightly higher total caloric and carbohydrate intake it came down to 160 mgm.

(3) Thyroid has the anomalous action of lowering blood sugar. Blood sugar estimations done after 14 days of thyroid therapy, and after prolonged thyroid therapy and a high caloric and carbohydrate intake, showed low blood sugar levels. The much lower figure for fasting blood sugar of 132 mgm. obtained in the latter case was probably due to the cumulative action of thyroid. After withdrawal of thyroid for one week the fasting blood sugar increased from 160 mgm. to 176 mgm., but this period was probably too short for the full manifestation of the withdrawal effect. These results are in keeping with the known fact of the slow-developing and cumulative action of thyroid. However, thyroid therapy and dieting have not lowered the blood sugar to normal levels; this may indicate that more accurate dosage was needed, or else the addition of some other (possibly endocrinal) factor.

(4) The hyperglycæmia was of the insulin-insensitive type. The caloric intake with insulin therapy was about the same as that when the carbohydrate was not less. The high insulin dosage of 40 units failed to reduce the hyperglycæmia. Moreover, the sugar levels shown after insulin and thyroid therapy were higher than with thyroid alone and a higher caloric and carbohydrate intake. This is difficult to explain.

My thanks are due to Miss S. Ram, lecturer in biochemistry, for her help and co-operation in doing the blood sugar investigation.

SURGICAL EMPHYSEMA AS A DIAGNOSTIC SIGN OF GASTRIC OR INTESTINAL PERFORATION*

By S. M. NAWAB

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A 17-YEAR OLD Hindu male was sent to the Arrah Sadar Hospital on 21st February, 1944, at 10-30 p.m. for a medico-legal report on his injuries which were considered trivial and had already been attended to at a district board hospital.

The patient appeared quite comfortable and unconcerned except for the fear of his impending trial. The pulse rate was 84 per minute; temperature 98°F. and respiration 18 per minute. On close questioning it was elicited that he was stabbed in a field about 16 hours before, while trying to steal some grain, and received two injuries, one on his abdomen and the other on his left thigh. The thigh injury was on the inner aspect of the lower part and, on exploration with a probe, its depth was found to be 1½ inches leading downwards, backwards and medially. The abdominal wound was 2 inches long on the front of the upper

part of the right side, and had been closed by 4 interrupted sutures. There was no tenderness or rigidity, no obliteration or liver dullness and both flanks were resonant. The only physical sign noted was the presence of surgical emphysema around the wound. A diagnosis of perforation of the stomach or transverse colon was made, and it was decided to undertake an immediate laparotomy.

Within an hour of admission, the abdomen was opened under general anaesthesia. The external wound was excised and enlarged in a transverse direction and the rectus muscle was divided along the line of incision. On opening the abdomen, the great omentum was found bruised and wrapped closely around a small perforation on the antero-lateral surface of the stomach near the pyloric end. It was closed with two layers of fine catgut sutures and covered by the omentum. The wound healed by first intention within 10 days.

A fortnight after the operation, however, the patient started running a mild temperature. Abdominal examination was negative but the part around the thigh wound was slightly tender. A few days later, a slight swelling with deep fluctuation could be elicited at that site, and it was decided to drain what appeared to be an infected hæmatoma. On 10th March, 1944 (17 days after operation), the hæmatoma was incised under local anaesthesia. A blood clot followed by a gush of fresh blood welled out. A tourniquet was applied immediately to the upper part of the thigh and the patient given general anaesthesia. The wound was enlarged and the popliteal artery exposed between the adductor magnus and semi-membranosus. A linear tear 1/3 inch in length was detected in the popliteal artery. Clamps were applied above and below the tear and the artery divided and sutured. All blood and clot were mopped out, 5 grammes sulphanilamide powder introduced into the wound, and the skin was closed by interrupted silkworm-gut sutures without drainage. The subsequent course was uneventful, and the patient was discharged cured on 2nd April, 1944.

Comments.—It is rather remarkable that both the blows which the patient sustained produced such unusual pictures. The presence of surgical emphysema around a chest injury is considered diagnostic of perforation of the underlying lung. It seems obvious that its presence around a wound in the abdomen should be considered diagnostic of perforation of a hollow viscus, but the author has failed to note this important sign described in any of the usual textbooks. The fact that injury to a hollow intra-abdominal viscus does not at least usually give rise to surgical emphysema in the abdominal wall seems to be due to the presence of the strong musculature of the abdominal wall which contracts firmly on receipt of an injury; hence air from the perforation more commonly escapes towards the liver, giving rise to the

* Rearranged by editor.

classical sign 'obliteration of liver dullness'. Again, while adhesions of the visceral and parietal pleura encouraging escape of air under the skin are common, they are much less so in the peritoneum between the visceral and parietal layers. Moreover, due to the absence of a rigid bony wall, the peritoneal cavity can accumulate a much larger amount of air or fluid than the pleural cavity.

I have to express my gratitude to the civil surgeon of Shahabad for permission to report this case.

A CASE OF GAS GANGRENE AND TETANUS TREATED WITH SULPHAPYRIDINE*

By K. C. CHAKRAVARTY, L.M.F., L.T.M.

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A HINDU male, aged 21 years, was admitted to hospital on 23rd June, 1943, at about 6 p.m. with a crush injury of the left hand sustained as a result of an accident while travelling in a lorry. Profuse hæmorrhage occurred during transit to hospital.

On admission, shock was present from both the accident and the hæmorrhage. The pulse rate was 128, respiration rate 27, and temperature 97.8°F. The muscles of the palm were completely lacerated with multiple fracture of the second and third metacarpal bones and also dislocation of the phalanges of the thumb. An immediate amputation at the wrist was decided upon, but the relatives of the patient strongly objected to this, though they were made fully aware of the dangers of gangrene and tetanus. In these circumstances, the wound was cleaned and all dirt, ragged muscles, broken pieces of bones were removed and the bleeding points were secured as far as possible under general anaesthesia. The ragged wound edges were apposed with loose stitches, maintaining free drainage. It was expected that the whole hand would slough off by degrees, and to check the possible danger of infection, sulphapyridine was given in an initial dose of 3 gm. within four hours of injury and 3 more grammes that day.

Next morning, the forearm swelled extensively up to the elbow and by the evening the swelling reached up to the armpit; the patient was toxic, and had a high temperature. The injured part was purple in colour and gave a slightly offensive odour with sero-sanguineous discharge. Gas gangrene was clinically diagnosed and a smear from the wet tissue revealed Gram-positive rod-shaped bacilli having spores resembling *Cl. welchii*; there were no facilities for culture. Tetanus antitoxin 3,000 I.U. was given prophylactically. Local treatment consisted mainly of 'dettol' baths for about an hour twice daily, with thorough cleaning and excision of devitalized gangrenous sloughs and broken bones.

On the third day, the swelling was oedematous, extremely painful, and crepitating, and the whole limb was emphysematous with a coppery red colour. Petechial hæmorrhagic patches and spots of different sizes were noticed under the skin. A seven-day course of sulphapyridine was now started with a total dosage of 5 gm. for the first, 4 gm. for the second, 3 gm. for the next three, and 2 gm. for the last two days. The swelling was found to be stationary next day, and there was less oedema. It was definitely subsiding, and most of the gangrenous muscles were falling off from the fingers from the third day of the course. The temperature became normal and the colour of the skin was looking healthy. The injured hand sloughed off at the palm except the fourth and little fingers, exposing a large area of unhealthy granulation tissue. The pain during dressing was intense, and the patient

and his relatives at last agreed to an amputation. The operation was to be done later when the patient's general condition improved.

Sixteen days after the injury, the patient first complained of pain in the teeth and difficulty in chewing. The mouth could not be opened more than three-quarters of an inch, and stiffness of muscles of the jaw was present. Examination of the mouth and throat did not disclose any cause. Tetanus antitoxin 6,000 I.U. was given immediately; no more was available. The symptoms were more marked by that night, especially pain during swallowing food, and rigidity of the muscles of the face and neck was seen. An amputation was undertaken next morning at the wrist through normal healthy-looking tissue. By the evening the patient developed all the cardinal signs of tetanus, e.g. risus sardonius, trismus, etc., and gradually, the typical generalized picture appeared. Reflex spasm of the whole body, though not very frequent, was present especially during feeding. To quieten the spasms hypodermic injections of magnesium sulphate 10 per cent were given, but even after three injections there was no effect; morphine, chloral hydrate and triple bromide were therefore given. As there was no certainty of obtaining antitoxin, the patient was given sulphapyridine in an initial dose of 1 gm. and 0.50 gm. every four hours for the first three days, and then 0.50 gm. every six hours for the next four days. From the third day, tetanus antitoxin became available. Two intravenous injections of 6,000 and 9,000 I.U. were given on that day; a dose of 20,000 units was given for three days and a final dose of 10,000 units. From the fourth day of tetanus the patient's condition appeared easier; tetanic symptoms began to subside gradually. On the eighth day the patient could open his mouth one inch and had no reflex spasm. The stump healed up within 15 days of amputation, and the patient was discharged 48 days after admission, a total of 91,000 I.U. of antitoxin, 17.50 gm. of sulphapyridine and sedative having been given.

Discussion

The drug of choice in tetanus is certainly large doses of antitoxin with the onset of first sign before the toxins are generalized. Antitoxin unless given in large doses (an initial dose as big as 200,000 is desirable), may not produce any effect. To quote Cole 'When toxin is exerting its effect on the nervous system, it is extremely doubtful if it can be neutralized by antitoxin; consequently if a lethal dose is so acting before antitoxin is given, this treatment cannot save the patient'. Bryant and Fairman used sulphapyridine in combination with evipan in tetanus with encouraging results. Cole however reported a desperate case in which sulphapyridine, in spite of combination with a fairly big initial dose (200,000 units) of antitoxin, failed to avert fatal termination. Ghosal and Chaudhuri in their series of cases used sulphapyridine in conjunction with evipan as a sedative; their cure rate was apparently 75 per cent, a record figure indeed. The antitoxin may have had a slight effect in the case recorded here in neutralizing toxin, but sulphapyridine seems to have exerted some action even without the aid of powerful sedatives such as evipan. Though not yet established as a specific against the clostridia group of anaerobes, sulphapyridine appears to be valuable in the treatment of gas gangrene and tetanus.

* Paper rearranged by editor.

In gas gangrene, though radical measures are needed to save life, one should consider well all the aspects of the case before deciding on the exact line of treatment. The presence of gas and swelling with change of colour does not always mean that the tissues are dead. The discovery of a suitable antibacterial agent would be a great help.

TWO CASES SHOWING CEREBRAL SYMPTOMS AFTER TREATMENT WITH QUINACRINE FOR MALARIA*

By J. N. BERRY, M.D. (Punjab)

Case 1.—A Hindu male, aged 25, had slight fever on 16th November, 1944, no fever on 17th but high fever on the 18th when I was called. The patient gave a history of previous attacks of fever relieved by quinine. Physical examination showed nothing abnormal but a hard spleen 4 fingers below the costal margin; temperature 104°F. Quinine sulphate mixture was prescribed for the first day followed by quinacrine, one tablet thrice daily for five days. The temperature came down the next day, but four days later the patient was seen very excitable, garrulous and behaving like a drunken man. As he was used to drinking, the symptoms were ascribed to it. However, the man accompanied a relative to the Wardha Hospital for emergency treatment, and while there he behaved similarly; he was very noisy and boisterous and was warded. In the morning he ran away but the next day he was reported to be in police lock-up for rowdyism. He was seen again on the 28th when he was quite calm and self-possessed and complained only of some sleeplessness; he stated that he had taken 4 quinacrine tablets before I was called and that the last tablet of the course prescribed was taken on the day the mental symptoms appeared.

Case 2.—A senior man on the technical staff, aged 30, got slight fever on 17th November, 1944, no fever on the 18th but high fever on the 19th when I was called. He had purged and starved himself the previous day in the hope of getting rid of fever without treatment. There was no abnormal physical sign except a hard enlarged spleen. He was diagnosed clinically as a case of malaria and was prescribed quinacrine tablets, one t.d.s. for five days. The fever came down next day, but on the 20th it rose to 103–104°F. but not afterwards. After finishing the course he went to work, but the next day (25th) he was seen to be very voluble and jovial and talking grandiose and impossible ideas. In the evening when I went to see him, he began talking incessantly; there was rapid speech and flow of ideas but without consistency or connection. It was ascertained that he was not used to drinking although his father was a drunkard. He was induced with some difficulty to take medicine and go to bed. He was treated as a case of acute mania with continuous sedatives (luminal and chloral with potassium bromide) and kept in bed for 48 hours. He practically recovered by 27th morning, and was allowed to attend work.

Discussion.—As far as I know, the Malaysians are thought to be the only hypersusceptible persons to quinacrine, and no such cases with cerebral symptoms have been reported from India. The two cases under report were noted during two weeks in the course of which about 200 to 300 cases of malaria were treated with quinacrine in this highly malarious area.

Both the cases had a predisposition to mental symptoms; the first was a drunkard and the second was of a hypochondriac nature.

Both had also a possible exciting factor, a sick relative in the first and domestic quarrel in the second; but these would appear to be too mild causes to produce such definitely pathological symptoms. Neither of them showed cerebral symptoms during the fever itself; nor was any big dose given; the first had 15 tablets and the second 18 tablets only. Both were cured of their mental symptoms in two to three days by sedatives and rest.

In spite of the cumulative effect of the drug due to delayed excretion, one would expect any symptoms due to it during its maximum concentration, i.e. during the first 24 hours after administration. The mental symptoms were noticed in the second case only after quinacrine administration had been stopped and at least 24 hours had elapsed between the last dose and the onset. These facts would appear to lend support to the hypothesis of malarial toxin causing cerebral and other symptoms propounded by Viswanathan in the *Gazette* of October 1944.

Summary.—Two cases of mental symptoms after quinacrine therapy for malaria are described and discussed.

STREPTOCOCCAL MENINGITIS IN AN INFANT TREATED WITH PENICILLIN*

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A CHILD, four months old, was admitted to hospital on 18th December, 1944, at about 10 p.m. for repeated convulsions since 9 p.m. Twenty days previously the child had pustular eruptions (itch?) on both legs; ten days later eruptions on the left hand and on the pinna of left ear, which probably acted as a source of infection. There had been fever for eight days.

On examination, heart sounds were rapid, pulse was feeble, harsh breath sounds were present in the lungs; the abdomen was soft; no rigidity of the neck or retraction of the head found; Kernig's sign absent; general condition not satisfactory.

Treatment.—That night sedatives, oxygen and cardiac stimulants were given. Next morning the child was still having convulsions; the anterior fontanelles were prominent and there was rigidity of the neck; the general condition was worse. Twenty-one c.cm. of cloudy cerebrospinal fluid under pressure were removed by lumbar puncture and a streptococcus was found in the fluid.

An intramuscular injection of 5 c.cm. of 20 per cent soluseptasine was given at 8 a.m. Convulsions occurred again at 10 a.m. Two hours later another lumbar puncture was done and 5 c.cm. of cerebrospinal fluid removed; 4,000 units of penicillin in 4 c.cm. were given intrathecally. There was one more convulsion two hours later after which the child slept fairly well. Another soluseptasine injection was given two hours later.

On the third day the child had no fits, took fluids by mouth fairly well and slept well. Lumbar puncture showed cloudy cerebrospinal fluid with no pressure; a few streptococci were seen. Rectal saline, oxygen and coramine were continued and another dose of penicillin was given.

Penicillin was continued for 5 days in the same dosage. Daily lumbar puncture showed no organisms

* Paper rearranged by editor.

* Paper rearranged by editor.

in the cerebrospinal fluid. The child gradually improved except for the recurrence of fit once again on the fourth day. Three weeks later the child appeared normal.

PROSTIGMINE IN A CASE OF PAROXYSMAL TACHYCARDIA

By R. C. SETH, M.B., B.S.

H. R., HINDU male, aged 62, farmer, came to me on 5th June, 1944, with a complaint of extreme breathlessness and throbbing in the chest, duration 3 days.

Family history.—Married 40 years ago. Has got six children. Father died at the age of 85 of some unknown cause. Mother died of paralysis at the age of 65.

Personal history.—Stout man weighing 2 maunds 30 seers. Still works in the fields. Smokes occasionally. Takes vegetarian diet. Does not drink.

Past history.—Gets attacks of palpitation and breathlessness for the last 20 years lasting from few hours to two or three days. The attacks used to come once or twice a year but now they occur nearly every month. The attack starts suddenly at any time mostly while at work and passes abruptly, occasionally after a vomit. He feels giddy during the attack with a sense of darkness before the eyes.

History of present illness.—Two days ago while he was working in the field he felt something jumping in his chest and soon became breathless. The condition is persistent since then. Active in between the attacks.

General examination.—The pulse rate could not be taken. Respiration 50 per minute. Neck veins prominent. No oedema. Apex beat not localized. Tic-tac rhythm with no differentiation in the sounds. No thrill or murmur. No enlargement of the liver. Apex beat counted with difficulty, 250 per minute approximately.

Treatment.—After all other devices had failed an intramuscular injection of prostigmine (Roche) 2 ampoules of 1.1 c.cm. each was given. After two minutes he felt nauseated, and suddenly the pulse which was rather imperceptible became full and bounding and came to 80 per minute. The respiration rate also slowed down to 20 per minute, and the patient walked out.

After a month he came to me with another attack, and again the same treatment was repeated, and he became all right after four minutes of the injection with a little vomit. There were no signs of myocardial failure. Since then, he has been taking prostigmine tablets by mouth $\frac{1}{2}$ tablet twice daily with no attack so far.

SULPHONAMIDES IN PERITONEAL SURGERY*

By P. N. LUTHRA, M.B., B.S. (Punjab), D.T.M. (Cal.)
Assistant Surgeon, Civil Hospital, Fazilka

ALTHOUGH according to Rendle Short, recent American experience is less encouraging, many favourable reports on the use of sulpha group of drugs introduced into the peritoneal cavity have appeared in the recent literature. The following case substantiates the claim.

A young girl in the third month of pregnancy was brought at midnight with eventration through a large stab wound in the abdomen. In one of the protruding

intestinal coils there were two small adjacent cuts through one of which a *Tænia saginata* had pushed out, quite one foot of its length, and was wriggling on the left breast of the patient, while the other end of the worm was visible from the second cut. The protruding gut was covered by a very dirty shirt worn by the patient. A large amount of dirt and some faecal matter which had gained exit with the worm contaminated the part.

The worm was dislodged, and the cuts in the small intestines were sealed with fine catgut. The gut after thorough cleansing and washing with sterile warm saline was placed within the abdominal cavity. Twenty c.cm. of 10 per cent soluseptasine was then introduced into the peritoneal cavity and the cavity was closed and stitched. For six days after the operation, the patient was given 10 c.cm. of 10 per cent soluseptasine intramuscularly morning and evening, and 100 c.cm. glucose saline intravenously twice daily. A flatus tube was passed whenever distension or pain in the abdomen was oppressing. For the first four days following the operation, she went through a stormy time with all the features of peritonitis but on the fifth day the quick low volume pulse improved, the temperature settled down and the vomiting and distension abated. She was then put on sulphonamide by mouth, 3 gm. a day for three days, and liquid diet was allowed and gradually increased. She made an almost uneventful recovery and was discharged three weeks after admission.

A CASE OF COMPLETE INVERSION OF THE UTERUS*

By N. P. GUPTA, L.M.F.

Medical Officer, Government Cinchona Plantation,
Rongo, Matelli, Jalpaiguri

ON the evening of 25th November, 1944, I was called to see a woman aged about 24 years, and the mother of two children, who had just given birth to a normal female child but the placenta had not been delivered. The child was lying in a pool of blood still attached to the cord. There was complete inversion of the uterus, and the placenta was partially attached to it. There was profuse bleeding from the uterus. The general condition of the patient was that of shock and hæmorrhage.

After treating the patient for shock, the child was separated from the cord. The placenta came out by a slight pull on the cord. The uterus was thoroughly washed with dettol lotion, but it could not be replaced and was still bleeding profusely. The cervical portion was in a contracted condition. A hot towel was applied over the part and adrenalin was applied locally over the fundus of the uterus with the expectation that it will act as hæmostatic and at the same time will contract the uterine muscle. The cervix actually relaxed as the fundus began to contract, and it was an easy job to replace the uterus in its normal position.

My thanks are due to Mr. P. W. Cresswell, Manager of the Government Cinchona Plantation, Rongo, for his kind permission to report this case.

A CASE OF VIPER BITE*

By B. L. CHOPRA

Divisional Medical Officer, Ferozepore

A KEYMAN of the N.-W. railway from Ferozepore city was admitted into this hospital on 27th September, 1944, four hours after having been bitten on the left little finger by a viperine snake, which also was brought after having been killed. Some first aid had been given to him.

On admission, the fang puncture was bleeding, the forearm was swollen and oedematous and the patient was complaining of severe burning pain. Pulse 90 per

* Paper rearranged by editor.

* Paper rearranged by editor.

minute, weak and thready; the extremities very cold; blood oozing from the gums, nose and eyelids with subconjunctival hæmorrhage.

First aid by incision and washing with potassium permanganate solution was given and a tourniquet was applied at the humerus. Concentrated anti-venom (polyvalent) serum 10 c.cm. intravenously and locally, calcium gluconate 10 per cent 10 c.cm. intravenously, and adrenalin $\frac{1}{2}$ c.cm. subcutaneously were given. Next day the anti-venom serum and calcium were repeated and an attempt was made to stop the bleeding from the gums and nose by plugging and application of adrenalin chloride diluted in normal saline.

The œdema and oozing continued. The site of injections also kept on oozing, with hæmatoma formation all round and blood was passed in urine and stools. Intravenous calcium was therefore stopped and subcutaneous injections of colloid calcium and ostelin 2 c.cm. and calcium gluconate 1 dram orally thrice daily were started. The bleeding stopped 8 days after the bite and the wound healed after two weeks. The patient was now very anæmic and was given iron mixture and, polyhæmin, pills. Five weeks after the snake bite the patient was enabled to resume duty.

A CASE OF ACUTE YELLOW ATROPHY OF THE LIVER*

By C. P. TANDON, M.B., B.S.

and

V. D. AGARWALA, L.S.M.F.

King Edward VII Hospital, Benares

A HINDU police constable, aged 28 years, was brought to this hospital on 27th October, 1944, at about 3 a.m. in an unconscious state, very restless and delirious and screaming at times. The history was that he got a severe headache at about 7 p.m. the previous evening for which his medical officer prescribed the usual A.P.C. powder, and six hours later he began to get delirious and very restless.

On examination, the tongue was dry; there were fine tremors in the hands; the pupils widely dilated, equal and not reacting to light; temperature 96.6°F., pulse 88 per minute; spleen and liver not enlarged.

Weil's disease was ruled out as there was neither fever nor enlargement of the liver and spleen. As the pupils were dilated, he was given treatment for dhatura poisoning, and after the stomach wash, etc., he actually quietened down.

In the morning he was still unconscious; pupils were slightly contracted but equal; slight icterus noticed in the conjunctivæ; blood pressure 146/80. Neck rigid; ankle clonus present but other deep reflexes deficient. A catheter specimen of urine showed the presence of bile and traces of albumin; a few pus cells and crystals of triple phosphate were also present. Blood picture showed nothing abnormal except for some poly-leucocytosis. Lumbar puncture revealed the cerebrospinal fluid under pressure (about 100 drops per minute); the fluid was clear, contained a little albumin but no micro-organisms or sugar.

The patient died that night without regaining consciousness.

On post-mortem examination, all the cutaneous tissues and meninges were stained yellow; the spleen, liver, kidneys, heart and lungs had petechial hæmorrhages; the lungs were deeply congested; the liver was small with a wrinkled capsule over it; the spleen was slightly enlarged; the gall-bladder was empty; the stomach contained a few ounces of coffee ground fluid; the intestines were green in colour; the blood vessels of the brain were engorged.

This case is interesting for its unusually short history, the absence of ætiological factors in the previous history, and the symptoms which were suggestive of dhatura poisoning.

* Paper rearranged by editor.

The authors are thankful to Lieut.-Colonel J. B. Vaidya, I.M.S. (retd.), for giving permission to publish this report.

[The diagnosis of this case appears obscure.—EDITOR.]

COMPOUND FRACTURE OF THE LEG WITH GAS GANGRENE TREATED WITH PENICILLIN*

By T. D. RAJOO

*Civil Surgeon and Assistant Medical Officer,
King Edward Memorial Hospital, Secunderabad
(Deccan)*

A PATIENT was admitted to hospital on the 24th December, 1944, with injury on his right leg due to a fall from a bullock cart. Examination revealed a compound fracture of both the bones of the right leg with gas gangrene spreading up to the lower portion of right iliac fossa. The patient's general condition was poor; he was toxic and the pulse rate over 140 and feeble.

Under a small dose of pentothal sodium, a guillotine amputation of the thigh was done as quickly as possible, and the raw surface was covered with septanilam powder and vaseline gauze and dressed with extension. Fifteen thousand units of penicillin were given intravenously in the theatre and continued every three hours; six injections were given intravenously and the rest intramuscularly. Anti-gas gangrene serum, 60,000 units intravenously on the first day and 30,000 units intramuscularly on the second day, were given. The patient rallied on the third day and has continued to progress since then.

I am grateful to my chief, Colonel L. K. Ledger, O.B.E., I.M.S., and to the military authorities for making penicillin available.

EMPHYEMA WITH CONTRA-LATERAL PNEUMONIA TREATED WITH PENICILLIN*

By K. U. THATAKIA, M.D.

B. J. Medical School, Poona

THE patient, aged 30 years, was admitted to hospital on 28th December, 1944, for right-sided empyema and left-sided pneumonia. Both the lesions were confirmed by screening.

As the patient was markedly dyspnoic and cyanosed on admission, 200 c.cm. of pus were aspirated. Bacteriological examination of the pus revealed staphylococci. 'Cibazol' was given, 4 tablets stat. and 2 tablets four-hourly. The dose was maintained for 4 days and then decreased. A total of 24 gm. were given in 5 days but the patient did not show any improvement; the temperature and the dyspnoea persisted. Three hundred c.cm. of pus were removed on 31st December, 1944, and 500 c.cm. again two days after.

On 2nd January, 1945, 20,000 units of penicillin were injected intrapleurally in 30 c.cm. of normal saline and this was repeated the next day. On the third day 15,000 units were given four-hourly. A decline in the temperature, a less toxic look and other signs of improvement began to appear from the fourth day. The pus was cleared as much as possible and a similar course of penicillin was repeated. Six days after treatment with penicillin the patient appeared quite well; the temperature which was swinging from 100 to 103°F. came down to 98°F.; there was no dyspnoea and no cyanosis. The patient was screened again; the right side of the chest was absolutely clear without any evidence of fluid and the left side showed a slight mid-zone haziness due to resolving pneumonia. The temperature continued to be normal and the pneumonia completely resolved afterwards. The sputum showed no acid-fast bacilli.

* Paper rearranged by editor.

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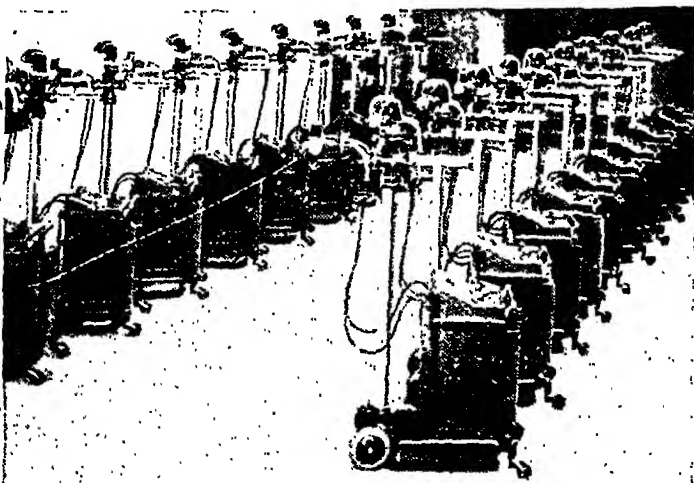
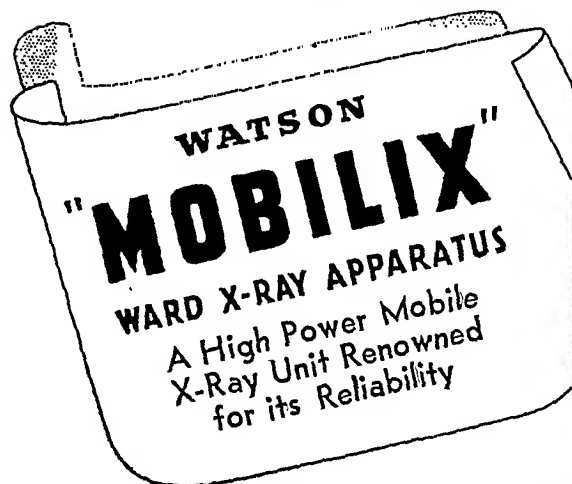
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APRIL

EXO-ERYTHROCYTIC FORMS OF MALARIA PARASITES

THE study of the development of malaria parasites in infected birds and men (and later in animals) has now been going on for over 50 years. The phase in the red cells, including the sexual and asexual forms, seems fairly clear, but it has always been uncertain what happens to the sporozoites injected by the mosquito before the forms in the red cells appear, and also it has been surmised that parasites might develop in cells other than red cells. One early view, expressed in 1893 by Golgi, was that parasites might undergo development in phagocytic cells in the internal organs and that these parasites might be immune to drug treatment. Later, Grassi in 1900 on the basis of morphological studies, suggested a phase of development intermediate between the sporozoite and the trophozoite. These early ideas were however considered to have been disproved by Schaudinn's published description in 1902 of the entry of sporozoites direct into the red blood corpuscles. Certain individual workers did continue to suggest that parasites might exist and multiply outside red blood cells, but they were a very small minority. Some workers failed to reproduce Schaudinn's findings. It was in 1931 and later that S. P. James focused attention once more on the possibility of exo-erythrocytic development of the malaria parasites. He noticed certain important differences between malaria induced by the bites of mosquitoes and malaria induced by the injection of a patient's blood containing trophozoites, and postulated that sporozoites underwent a phase of development in connective tissue cells or endothelium. The main difference between malaria induced by the two methods was that malaria induced by injection of blood could sometimes be prevented by quinine administration, that the fever could be much more readily controlled, and that relapses less frequently occurred than in malaria due to bites of infected mosquitoes. This indicated, after infection by mosquito bites, the occurrence of the parasite in a special form more resistant to drugs. Later, work on the synthetic anti-malarials gave support to this idea, and the fact that plasmodium could sometimes prevent malaria following infected mosquito bites and also appeared to reduce the tendency to relapse, suggested that this special form, more resistant to drugs, might be affected by plasmodium and not by quinine or atabrin. These ideas were supported by various eminent workers including Warrington Yorke.

But actually even before 1931, reports had been made, in avian malaria, of parasites occurring and multiplying in cells other than the mature erythrocytes. Such a report had been made in 1923 by Ben Harel; later reports by Raffaele appeared in 1934. From that time onwards, numerous workers have recorded the occurrence in bird malaria of these exo-erythrocytic forms of the parasite, and the literature of the subject is now attaining very large proportions.

It is now generally agreed that the exo-erythrocytic forms can give rise to the erythrocytic forms and vice versa. This view makes it difficult to understand why there should be such a difference as has been reported between malaria induced by infected blood injections and malaria produced by mosquito bites.

Porter and Huff in November 1940 published a good survey of the literature bearing on this subject and quoted no less than 109 references, and since then the number of references has gone up greatly. The summary of Porter and Huff's article is as follows:—

Large, non-pigmented schizonts manifestly different from the classical schizonts found in erythrocytes have been observed in some strains of *P. relictum*, *P. gallinaceum*, *P. cathemarium*, *P. circumflexum*, and (one unconfirmed report) *P. nucleophilum*, but not in several other species of avian and simian malaria examined. Although human malarial infections have not yet been extensively studied, forms similar to those seen in avian malaria have been reported in infections with *P. vivax* and *P. falciparum*.

The identification of infected cells has usually not been made by specialists, but infections are reported in endothelial cells and various cells of the lymphoid-macrophage system (rarely in granulocytes).

In infections with *P. elongatum*, schizonts occurring in all blood and blood-forming cells are morphologically identical; the large schizonts mentioned above have not been described.

That the exo-erythrocytic schizonts are a part of the malarial life cycle and not a contaminant, is indicated principally by the facts that they have not been separated from malaria nor shown to occur apart from it, that they differ characteristically in different species of malaria, and that their immunological specificity parallels that of the associated malaria. Miscellaneous other evidence supports this view. They clearly differ from both avian and mammalian types of toxoplasms in morphology and transmissibility.

The exo-erythrocytic stages are not appreciably affected by schizonticidal drugs, but their number is reduced by plasmodium.

Various evidence that the sporozoite development does not occur in circulating erythrocytes, together with the fact that the exo-erythrocytic schizonts appear earlier and more numerous after sporozoite inoculation than after the injection of infected blood, suggests that the exo-erythrocytic schizonts are the early developmental stages of sporozoites. Evidence is inconclusive on this question, though exo-erythrocytic schizonts have been found 16 hours after the inoculation of sporozoites.

Other ideas on the significance of the exo-erythrocytic stages include theories that they reflect an unfavourable condition of the blood as a medium, or reduced digestive activity of tissue phagocytes, and the theory that they represent stages in the evolution of sporozoa of the sub-order *Hæmosporidiidea* into strictly erythrocytic parasites. While they indicate a closer relationship between the *Plasmodiidae* and the *Hæmoproteidae*, adequate criteria for the separation of these families still exist.

In addition to their great biological significance, the newly discovered exo-erythrocytic stages are of vital importance, particularly in the study of chemotherapy of malaria.

It is true that some workers have challenged the accuracy of some of the observations reported. It is also true that the proof of the existence of this form of the parasite in bird malaria does not also prove the occurrence of similar forms in human malaria. Nevertheless, it seems that they probably do occur in human malaria, and actually several reports of the demonstration of such parasites in human beings have been made, although they have not yet obtained general recognition.

It may be asked why there should be so much difficulty in demonstration. In discussing this matter recently S. P. James wrote as follows:—

'Their origin, development and clinical and pathological effects can be observed with least difficulty in the domestic fowl. A good way in which to begin to study them is to inoculate sporozoites of the parasite *P. gallinaceum* on the chorio-allantoic membrane of chick embryos at about the tenth day of incubation of the eggs. After a drop of normal saline containing the sporozoites has been dropped on the membrane, the window that has been made in the shell is closed with a coverglass and plasticine, and the eggs are returned to the incubator for a few more days or until the chick hatches out, or is about to do so. By making smear preparations from the brain, spleen and liver of one or more embryo chicks on different days after infection, one finds the schizogonic forms in cells of those organs and in leucocytic cells and monocytes in the blood. Rare, but quite unmistakable, forms can be found in those tissue cells several days before any parasite can be found in red blood corpuscles. This proves, of course, that they are the first event in the life history of the sporozoites which were inoculated. The longer one continues incubation of the eggs after their inoculation, the more numerous the schizonts become until, by the day on which the chick is due to hatch, several forms are present in every field of the microscope. By that time, too, the red cells have become heavily infected with merozoites produced by the sporulation of the schizonts, and the chick dies from the severity of the infection either before, or shortly after, it has succeeded in emerging from the shell.

Evidently these very young chicks are much more susceptible to the parasite than older birds. This is also true in human malaria as is shown by comparing infections in new-born babies with those in adults. The infection in chickens is always fatal to those under 2 weeks of age and it is fatal by the severity of the exo-erythrocytic infection rather than by that of the red cells. In fully grown and old birds the reverse is the case as it is often difficult in those birds to find any exo-erythrocytic parasites although one knows that they must have been present to start the red cell infection.

So, if one were to set out to try to find these forms in human malaria the odds would be perhaps a thousand to one against success in any case except that of a baby heavily bitten by infected mosquitoes just after it was born. I mention this to counteract the conclusion which some observers have made that exo-erythrocytic schizogony does not occur in the human malaria parasites because they have failed to find it.'

As is stressed by James and many other writers on the subject, including Porter and Huff quoted above, this matter is of vital practical importance in the prevention and treatment of malaria. The indications are that

this form of the parasite is not affected by quinine or atabrin but that it probably is affected by plasmochin. It is now possible to grow the exo-erythrocytic form of avian parasites in the chick embryo and in tissue culture, and an attempt is now being made to study the action of drugs on these parasites in these cultures. It appears that the only anti-malarial drug to have any effect upon it is plasmochin. This work however is in its early stages. It has been the subject of preliminary reports by Hawking.

These findings lend support to the idea that of the anti-malarial drugs the only one which has any action in preventing the transmission of malaria by the mosquito bite is plasmochin, but unfortunately the dose needed is too large to make this a generally applicable measure, for plasmochin is a toxic drug. The possibility of finding by tissue-culture work a less toxic drug which will have a lethal action on the exo-erythrocytic forms is however not negligible, and the work is obviously of great importance.

Moreover, numerous workers have expressed the view that it is the persistence of this drug-resistant form in the body which gives rise to the late relapses of malaria. In the past, the difficulty or impossibility of preventing relapses by the administration of large doses of quinine for long periods has been demonstrated by many experienced workers, Warrington Yorke being a great exponent of this view. If the persistence of the exo-erythrocytic form of the parasite is the cause of the relapse, then this is easily understandable, and there is a body of opinion which adopts the view that the problem of prevention of relapse will be solved only when a non-toxic drug which is effective against the exo-erythrocytic form of the parasite has been discovered. Experience in human malaria in the past has indicated that plasmochin does appear to reduce the relapse rate, but that the dose needed is rather high, perhaps too near the toxic dose. This observation now appears to be perhaps explainable by the fact that plasmochin is the only drug yet shown to have any action against the exo-erythrocytic forms of the parasite.

For the present, this discussion must end here. The confirmation of the existence of the exo-erythrocytic forms of the human malaria parasites is not yet available. The proof that the drug-resistant properties of these exo-erythrocytic forms are the reason for the failure to prevent malarial infection by drugs is not yet complete. The idea that the exo-erythrocytic form can persist for long periods and cause late relapses is only a hypothesis. We await the completion of these proofs and the discovery of a drug which will rapidly eliminate these exo-erythrocytic forms. If these proofs and discoveries are forthcoming, many of the unsolved problems of malaria will be on their way to solution. The developments of

the next few years or even months are awaited with interest.

J. L.

SULPHONAMIDES IN URINE

A SIMPLE TEST FOR DETECTION

WHENEVER treatment with sulpha drugs is undertaken, it is important to ascertain whether the patient has already taken any, so that adequate but not excessive dosage may be given. A patient may be quite ignorant of its previous administration; he may come in a confused state without a medical report; or the report may indicate that the drug was prescribed but it was not actually taken. In such circumstances, we need to test the blood or urine to obtain definite evidence whether the drug had been taken previously or not, as it is never present in the body unless previously taken.

There are several tests for the purpose; the simplest of these is the lignin test (Hallay, 1942). Lignin, a constituent of wood, is present in wood-pulp papers such as newspaper, toilet paper or paper towels, but not in 'purified' papers such as filter paper. For the test a drop of urine is placed on a piece of newspaper and one drop of 5 per cent hydrochloric acid added. A yellow colour appears immediately which deepens to an orange with higher concentrations. The exact chemical reaction responsible for the change of colour is obscure, but fortunately other substances which may give a similar reaction do not occur in the urine.

Bogan (1943) obtained very satisfactory results with the test after extensive trials. The test was applied as a routine to every sample of urine examined in the Norfolk Naval Hospital along with microscopical examination of the centrifuged deposit for sulphonamide crystals.

'Analysis of the results in the first 3,000 specimens of urine tested revealed positive chemical tests for sulphonamides in about one-eighth of the urines, of which about one-fifth showed sulphonamide crystals, usually acetylated sulphathiazole, microscopically. More than half of the specimens received from the pneumonia service gave positive tests, with more than a third of them showing crystals in the urine, and the negative tests were mainly from new admissions or patients already convalescent, etc. Only a half dozen specimens of the 3,000 tested were reported to have sulpha crystals microscopically without a positive chemical test. Unfortunately, the specimens were not saved for check in any one of these cases, in order that the exact nature of the crystals seen could be identified, but it seems probable that they were cases of mistaken identity rather than false negative tests.'

The concentration of sulphonamides is indicated according to the intensity of the colour as follows:—

Colour	Read as	Approximate per cent
Faint yellow ..	+	0.01
Deep yellow ..	++	0.05
Orange yellow ..	+++	0.1
Orange ..	++++	0.5 or more

As a simple qualitative test which can be carried out by the bedside, it is of great practical value and deserves wide publicity.

R. N. C.

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Special Article

THE CAUSATION OF CANCER WITH SPECIAL REFERENCE TO ENDOCRINE INFLUENCE

By ERNEST F. NEVE, M.D., F.R.C.S. (Edin.),
F.R.C.S. (Eng.)

IN the July number of *Surgery*, an American monthly journal, there is an interesting symposium on 'Endocrinology of neoplastic diseases.' This consists of nine articles by distinguished surgeons and pathologists attached to various American schools of medicine including Harvard and the Johns Hopkins. The following is a short summary of the interesting articles:—

The prostate gland is the commonest site of neoplastic enlargement. Dr. Robert Moore of St. Louis in discussing benign hypertrophy and carcinoma of the prostate gives references to 42 monographs on the subject. The effect of castration was long ago mentioned by John Hunter. Towards the end of the 19th century, both in Great Britain and America, castration was widely performed for benign enlargement. It has been shown that by this operation prostatic carcinoma undergoes considerable improvement. It would therefore appear that both the benign and carcinomatous hypertrophy are endocrinological dystrophies. Dr. Moore mentions that there are a few cases on record of complete destruction of the pituitary by a supra-sellar cyst, in which histological examination of the prostate showed complete atrophy; on the other hand, in cases of adrenal insufficiency there is a tendency to hypertrophy of the prostate. It is however the androgen influence of the testis which is most important. This is still further indicated by the fact (quoted by Moore) that in 28 eunuchs who lived to be over 45 years of age there were no signs of benign prostatic hypertrophy as compared with the normal incidence of about 50 per cent. In individuals with pituitary infantilism there appears to be a similar immunity. Dr. Moore also reviews the results of experimental production of the two conditions in

animals, and experimental work on animals to find out the effect of injections of androgens and estrogens. Schenken and Burns demonstrated that the administration of stilboestrol (a synthetic estrogen of the ovarian follicle type) continued over periods up to 69 days in man, brought about profound degenerative changes in the neoplastic cells of carcinoma of the prostate, demonstrable by serial biopsy. It has been claimed by others that the addition of a hormone extracted from the epididymis accentuates this action.

Dr. Howard Taylor discusses tumours of the uterus and endocrine factors. Here, as in the case of prostatic neoplasms, it has long been known that castration may cause shrinkage or even disappearance of benign tumours, and that, *a priori*, certain substances formed in the ovary were in some way responsible. Experiment on animals has confirmed this and demonstrated the protective effect of hormones derived from the corpus luteum. The presence of ovaries or even parts of them, and the absence of corpus luteum, favours hyperplasia of the endometrium, which however injections of follicle estrogens have difficulty in producing if corpus luteum hormone (progesterone) is employed at the same time. There is very little evidence of endometrium hyperplasia going on to carcinoma; nevertheless there is evidence for an estrogen factor in endometrial cancer, for many patients have been observed with associations of a granulosa-celled tumour of the ovary with adenocarcinoma of the endometrium; these and the theca-celled ovarian tumours have a definite estrogen-producing capacity.

Emil Novak from the Gynæcological Department of the Johns Hopkins Medical School contributes an article on ovarian tumours with sex hormone function. Novak describes a group of ovarian tumours which possess the property of producing male or female sex hormones. Incidentally, this profoundly modifies the older view that cancerous tumours are made up of parasitic cells which have cut themselves off from all functioning activity except growth. For such tumours have relationship not only to endocrines with regard to their production but may also themselves produce certain secretions. For example, the cells of certain hepatic carcinomas may produce bile, while mucin is produced by the cells of some intestinal carcinomas. There are certain ovarian tumours classified as arrhenoblastoma having their origin in embryological life, which contain testicular cells and which have the capacity of producing male sex hormone. This neoplasm is termed 'ovarian dysgerminosa'.

The relationship of hormones to diseases of the breast forms the subject of another article by Dr. Ira T. Nathanson from Harvard Medical Laboratories. It has long been known that hormones are concerned in mammary development and function, so obviously they may have

relation to the production of benign or malignant diseases of the breast. It is now generally accepted that by injections of estrogens (ovarian follicular hormones), duct systems can be developed in the breasts of animals and even man. In monkeys and guinea-pigs, lobule and alveolar growth occurs as well. Hormones, both of the adrenals and the pituitary, have also been shown to stimulate mammary growth. A series of experiments have established the importance of heredity in the development of tumours in mice. Lacassagne in 1932 succeeded by the administration of estrogen in producing cancer of the breast even in male mice. Geschichte has reported a high incidence of mammary cancer produced by prolonged administration of estrogens in rats.

This work has indicated that estrogens should not be used in any form in large doses or over a long period of time where there is a family history of cancer, or in any case of chronic mastitis or any form of neoplasm, either before or after surgical or radiation treatment. If used at all, there should be initial and repeated examination of both breasts. Oophorectomy has been suggested as part of the treatment of breast cancer, and it has frequently been attended by alleviation of symptoms and signs. Of late years, *x*-rays have been substituted. The chief improvement however has been in the bone metastases which in a good many cases regressed or disappeared.

To sum up, the causes of cancer are predisposing and exciting. Recent research has thrown light on predisposing causes such as heredity and lack of endocrine balance. Of the exciting causes, irritation is by far the greatest. This may be direct such as mechanical of which the rapid *x*-ray, radium and heat waves are examples. Chemical irritants such as betel chewers' cancer in India, certain epitheliomata arising in industries where the skin of workers is exposed to friction, association with chemical irritants, and the cancer produced in rats by continuous application of coal tar. Indirect irritation may arise from glandular ducts blocked by debris, especially in the breast or from the result of injury or former wounds. This latter if occurring in mesoblastic tissue is apt to result in sarcoma.

One direction in which experimental work might be carried on with great advantage would be the influence of diet upon the production of hormones or their products. The introduction of the Allen Doisy test making the measurement of estrogenic activity possible, and the study of hormone excretion through the urine should facilitate this. McCarrison's research work threw much light upon the causes of certain digestive ailments. Has excess of proteins or of other items of diet any effect on hormone balance? Another more difficult line of research is that into the nervous control of endocrines and trophic nerve control of tissue growth. We know so little about this.

Medical News

POST-GRADUATE COURSES IN TUBERCULOSIS

WITH a view to securing the co-operation of general medical practitioners in the fight against tuberculosis in the country, the Tuberculosis Association of India has drawn up a programme of post-graduate refresher courses in tuberculosis in different parts of the country. A course of one month's duration will be held in June next consisting of lectures and demonstrations at Madras and Arogyavaram, and a visit to Perundurai Sanatorium. Registered medical practitioners—both men and women—will be eligible for admission to these courses.

THE FACULTY OF TROPICAL MEDICINE AND HYGIENE, BENGAL

THE following students are declared to have passed the D.T.M. Examination, Session 1944-45 :—

Passed

(Arranged in alphabetical order)

- Dr. Keshab Lal Baishyasaha, L.M.F., L.T.M. (Bengal), Clinical Pathologist, Police Hospital, Calcutta.
- Dr. Amal Kumar Banerjee, M.B. (Cal.), Private Practitioner.
- Dr. Gadadhar Krishna Banerjee, M.B. (Cal.), Medical Officer, Empire Jute Mills, Tittaghar.
- Dr. Santosh Kumar Basu, L.M.F., L.T.M. (Bengal), Sub-Assistant Surgeon, Bengal Nagpur Railway.
- Dr. Saradindu Chakrabarty, M.B. (Cal.), Private Practitioner.
- Dr. Arun Kumar Chakravarty, M.B. (Cal.), Private Practitioner.
- Dr. Nirmal Chandra Chakravorty, M.B. (Cal.), Private Practitioner.
- Dr. Girija Mohan Chatterjee, M.B. (Cal.), Medical Officer, The Britannia Engineering Co., Tittaghar.
- Dr. Jogeswar Chatterjee, L.M.F. (Bengal), Leprosy Medical Officer, Barakar.
- Dr. Niranjan Chatterjee, M.B. (Cal.), Medical Officer, Ganges Rope Co., Ltd., Howrah.
- Dr. Chen Tzu Ta, M.B. (China), Visiting Physician, Kwisyang Central Hospital.
- Dr. (Mrs.) Gladys Connor, M.B., B.S. (Mad.), D.M.C.W. (Cal.), Private Practitioner.
- Dr. Ajit Kumar Das, M.B. (Cal.), Medical Officer, A.R.P. Depot, Calcutta.
- Dr. Sailendra Nath Das, M.B., D.P.H. (Cal.), Assistant Bacteriologist, Corporation of Calcutta.
- Dr. Sankar Prosad Das Gupta, M.B. (Cal.), Private Practitioner.
- Dr. Kali Charan De, M.B. (Cal.), Private Practitioner.
- Dr. Triguneswar Ganguly, L.M.F., L.T.M. (Bengal), Sub-Assistant Surgeon, Bengal Nagpur Railway.
- Dr. Harbans Singh Gill, M.B., B.S. (Lahore), Private Practitioner.
- Dr. Krishan Singh Grover, M.B., B.S. (Lahore)—Awarded the 'Chuni Lal Bose' Gold Medal 1945, Private Practitioner.
- Dr. Mohammed Afzal Hosain, M.B., B.S. (Lahore), Private Practitioner.
- Dr. Suchandra Prasad Jain, M.B., B.S. (Lucknow), Medical Officer In-Charge, Medical Wards, Irwin Hospital, New Delhi.
- Dr. Dev Raj Khurana, M.B., B.S. (Lucknow), Honorary House Surgeon, Irwin Hospital, New Delhi.
- Dr. Liu Chun Hsiang, M.B. (China), Assistant Expert, National Epidemic Prevention Bureau, Kunming.
- Dr. Ma Lung-Shui, M.B. (China), Health Officer, Chinese Government.
- Dr. Provat Kumar Mallik, M.B. (Cal.), Medical Officer, Anti-Leprosy Unit, Purulia.

- Dr. K. P. Bhaskara Menon, M.B., B.S. (Mysore), Honorary House Surgeon, District Hospital, Quilon, Travancore.
- Dr. Joseph Morgan, L.C.P. & S. (Bom.), Medical Officer, T.B. Sanatorium, Wanlesvadi.
- Dr. Rabindra Nath Mukherjee, M.B. (Cal.), Medical Officer, Ballygunj Charitable Dispensary, Corporation of Calcutta.
- Dr. Shakti Proshad Mukherji, M.B., B.S. (Patna), Assistant Surgeon and A.R.P. Medical Staff Officer, Govt. of Bihar.
- Dr. Thopalle Suryanarayana Murty, M.B., B.S. (Vizag.), Private Practitioner.
- Dr. Basudeb Nath, M.B. (Cal.), Private Practitioner.
- Dr. Pan Hsiu Ming, M.B. (China), Health Officer, China.
- Dr. Amiya Kumar Roy Chowdhury, M.B. (Cal.), Private Practitioner.
- Dr. Sudhanwa Kumar Saha, L.M.F., L.T.M. (Bengal), Private Practitioner.
- Dr. Bhupati Bhusan Sarkar, M.B. (Cal.), Medical Officer, Gondolpara Jute Mills, Chandernagore.
- Dr. Sudhindra Nath Sen, M.B., B.S. (Patna), Private Practitioner.
- Dr. Mundrika Prasad Sinha, M.B., B.S. (Patna), Private Practitioner.
- Dr. Ratneshwar Prasad Sinha, M.B., B.S. (Patna), Private Practitioner.
- Dr. Tai Tih, M.B. (China), Medical Officer, Chinese Air Force.
- Dr. Abani Mohan Tarafder, M.B. (Cal.), Private Practitioner.
- Dr. T. K. Velayyapillai, D.M. & S. (Mad.), Private Practitioner.
- Dr. Amar Kumar Varma, M.B., B.S. (Lucknow), Private Practitioner.

CASES OF ŒDEMA IN BENGAL

DURING and after the Bengal famine, cases of œdema were numerous and general anasarca was a common cause of death. The clinical picture of these cases is described elsewhere in this issue. Hypoproteinæmia and changes in the albumin-globulin ratio, were constant features, and enlargement of the liver with mild degrees of cirrhosis was also a common finding. Contrary to expectation, clear-cut vitamin deficiencies were very rarely seen and the evidence was that vitamin-B₁ deficiency was not a common and important cause of œdema.

In view of reports that cases of œdema were still common in Bengal villages the desirability of a study of the matter was realized. The existence of the Singur Health Unit near Calcutta established by Dr. John B. Grant provided facilities for the study of this matter in that area. The study was carefully planned and carried out and the report has reached us written by Drs. P. C. Sen and S. C. Seal of the All-India Institute of Hygiene and Public Health. The report describes in detail the methods used including ascertainment visits, diagnostic visits, filling in of schedules, physical examination and examination of clinical material, dietetic survey, economic survey, etc., and gives details of the different schedules used. The report then presents the findings of the investigation. Actually the œdema cases in the area of Singur Health Centre appear to be few, and the report describes only one group of cases found in one village, the cases numbering 9. Five of them showed clinical picture of epidemic dropsy; examination of the mustard oil used in these houses confirmed the diagnosis. In the other four cases the clinical picture was not that of epidemic dropsy and the signs and symptoms varied considerably, some showing tongue lesions, some showing anæmia, one showing enlargement of the heart, three showing cardiac irregularity, some giving history of diarrhoea and so on. A study of these cases and the dietary of the cases showed that the œdema was associated with or caused by vitamin deficiency, particularly vitamin B₁. The report ends by pointing out that the causes of œdema in cases found in Bengal villages are various.

Public Health Section

AN EXPERIMENT IN RURAL MEDICAL RELIEF

By A. T. W. SIMEONS, M.D.

Director of Public Health, Kolhapur State

THE question of providing rural medical relief is receiving great attention throughout the country. Although a number of different schemes have been tried, none have, to my knowledge, proved very satisfactory. It was, therefore, decided to make an experiment with what we call 'rural sub-dispensaries' run by laymen who have received a short course of training. It was also decided to make a small charge for the medicines, but no fees were to be charged.

The system works as follows:—

(1) Villages with a population of over 1,000 inhabitants, or groups of smaller villages, are visited and encouraged to apply on a prescribed form for the opening of a rural sub-dispensary. In the application they agree to provide a clean, well-lit, well-ventilated and centrally situated room, with furniture. They agree to choose from among themselves candidates for training from whom the D.P.H. selects the most suitable one. The qualifications entitling a person to the candidature are that he must be a respectable permanent resident of the village with an assured income and an education not less than Vernacular Final. The choice must be approved by the patel, the president and the members of the *gram panchayat*, and other prominent villagers.

(2) When a candidate is approved, he must at his own expense (or at the expense of the village) spend 14 days in Kolhapur City for training. He is given a vernacular textbook specially written for this purpose.* During their training, much time is devoted to teaching them to recognize diseases which they are not allowed to treat and which they must immediately refer to a qualified doctor. It is made very clear to all sub-dispensers that they can in no way consider themselves entitled to 'practice medicine.' They are taught to regard themselves as agents for the supply of Government remedies. Great stress is laid on this point, to counteract one criticism the scheme has evoked, namely, that it encourages quackery.

(3) At the end of the training, the candidate appears for a short *viva voce* examination in which he is only required to show that he has

fully mastered the contents of his textbook and has acquired the necessary proficiency in dressing wounds, taking temperatures, keeping tidy records, etc. If he passes, he is given a certificate entitling him to work in Kolhapur State as a rural sub-dispenser.

(4) Rural sub-dispensers are paid an honorarium of Rs. 5 per month. They are bound to keep the dispensary open for at least half an hour every day. No dispensary may remain closed longer than 48 hours, including holidays, without a written application for leave having been sanctioned.

(5) Rural sub-dispensers are strictly forbidden the use of any kind of drug, medicine or medical appliance other than those supplied to them by Government. They are not allowed to treat cases in any way other than described in their textbook. Diseases which are not covered by this textbook may not be treated by them. They are not allowed to take any form of fee. They are not obliged to attend patients outside dispensary hours nor to visit the sick in their homes. They are, of course, free to do this if they wish, but they cannot charge any fee for such services.

(6) The prices of medicines have been fixed in such a way that on an average 1 to 3 days treatment costs one anna. This money is collected from the patients. In some cases this price exceeds the actual cost of the medicine; in others it is less. The set of medicines supplied and the instructions given with them have been arranged in such a way that as a rule the income from the sale of drugs balances the expenditure. In fact, in most dispensaries, there is a slight surplus. As far as possible, medicines are supplied in tablet form or in ready-packed powders, but in any case the sub-dispensers do not do any compounding. All drugs have been given colloquial names and the sub-dispensers are not taught their composition.

(7) Sub-dispensers have to maintain a careful register in which they enter the symptoms—not the diagnosis—of every case, and all other particulars regarding treatment, payment, etc. They also have to maintain a stock book. They are given printed indent forms, which they send in duplicate to the Public Health Department for fresh supplies with the equivalent in cash.

(8) Each group of 25 sub-dispensaries is visited, controlled, and supervised by a full-time inspector of sub-dispensaries who is a registered medical practitioner. His pay is Rs. 60 p.m. plus Rs. 45 A.T.A. His duty is to give advice in difficult cases, to check cash, registers and stocks and to see that the regulations regarding treatment outlined in the textbook are rigorously adhered to.

*This textbook has been published in Marathi. It contains chapters on 'Rules and regulations' governing sub-dispensaries; instructions on record, book and stock keeping; a detailed description of each medicine supplied, giving its use, dosage, indications, etc.; an index of the commonest illnesses with instructions how to recognize and treat them. It is written in the plainest possible style.

The cost of running such rural sub-dispensaries is as follows:—

(1) Initial cost of installing, equipping, training, etc., approximately Rs. 100 per dispensary.

(2) Maintenance cost including pay of inspectors, and the office staff at headquarters, is roughly Rs. 100 per dispensary, annually. The cost of subsequent indents for medicines is fully covered by the income from the dispensary.

As an experiment, 10 such sub-dispensaries were opened 8 months ago in Kolhapur. Of these, two had to be closed down, the one, because the sub-dispenser left the village and the other, because, on the first inspection, serious financial irregularities were discovered. The remaining 8 sub-dispensaries worked so satisfactorily that a further 22 were opened 4 months later. In all, 30 sub-dispensaries are now operating and another 30 are about to be opened.* The average monthly attendance is 150 per dispensary. Some enthusiastic sub-dispensers have 400 to 500. The success of these rural sub-dispensaries is further demonstrated by the large number of applications coming in from villages all over the State, asking for the opening of a sub-dispensary.

The Kolhapur Government has now decided to sanction this plan as a permanent institution of the State. The Public Health Department is extending the scheme as rapidly as possible. By the end of 1945, about 150 sub-dispensaries will be established. It is planned to provide every village in the State having more than 1,000 inhabitants, with a rural sub-dispensary. This will mean that 300 such sub-dispensaries will be established, which will require 2 years, and that each will serve an average of about 3,500 inhabitants, involving an annually recurring expenditure of less than Rs. 30,000.

Rural sub-dispensaries are preparing the ground upon which a qualified medical practitioner will later be able to thrive in rural areas.

In a few of the villages where rural sub-dispensaries have been established, there are already qualified doctors in practice, and it was at first feared that their practice might suffer through the opening of a sub-dispensary. Experience has, however, shown that this is not the case. On the contrary, established practitioners are getting more patients, because sub-dispensers have strict instructions to refer all serious cases to qualified men. In almost every case the resident practitioners have, after initial scepticism, found that the establishment of a sub-dispensary has improved their practice and their standing.

The scheme is still very young, and much further experience will have to be gained, but it was thought that any concrete suggestion which experience has shown to be workable should be made known now.

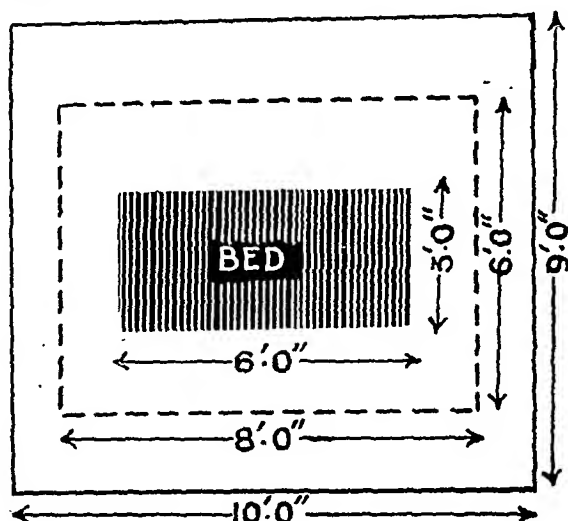
*This has now been done.

SKETCH OF A MOSQUITO-PROOF ROOM

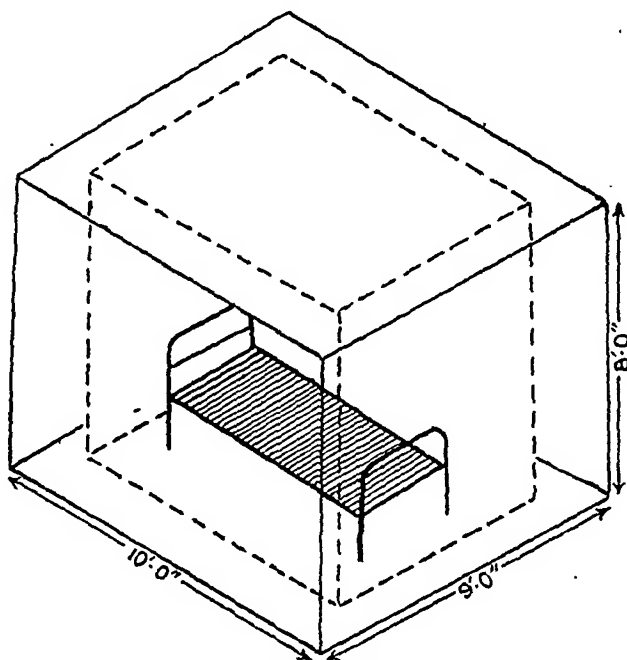
By A. H. HARTY
COLONEL, I.M.S.

Inspector-General of Civil Hospitals, C. P. and Berar

AMONG the provisions of the yellow fever regulations, is one that there must be, in each area, a mosquito-proof building to accommodate patients suffering or suspected to be suffering from yellow fever, but I believe that owing to the difficulty in obtaining fine wire gauze it has not been possible to construct many of these mosquito-proof buildings or even rooms.



PLAN



ISOMETRIC VIEW

As an alternative, I have devised a cheap room made from ordinary mosquito-curtain material for use in the Central Provinces; and

I believe it to be efficient and safe in the hands of careful doctors and nurses. The rough sketch shows at a glance the construction of it. It is a room inside a room with a corridor or space all round, the measurements being: outer room, length 10 feet, width 9 feet and height 8 feet; inner room, length 8 feet, width 6 feet and height 8 feet. The skirting is weighted by small sand bags sewn at intervals along the lower border.

The nets which are sewn together along the roof only should be suspended by tapes from wires or ropes tightly stretched across the room and the skirting should lie on the floor. Nurses and attendants are to enter and leave by lifting up one net at a time. After actual trial, it has been found that several mosquitoes succeed in getting inside the outer room and a few into the inner room but they are easily killed by flit if nurses entering in the room make it a point to flit them as soon as they are seen in either of the rooms. The important thing is not the mosquitoes that enter but those that escape from the rooms after having fed on the patient inside; these will infect other persons, so it is important that every mosquito trapped should be killed as soon as it is seen.

A simple net of this design was made for Rs. 62 from the ordinary cotton mosquito-curtain material, and it has been tested by two differing civil surgeons by actually nursing patients in it. I am indebted to Colonels D. Kelly and W. Scott for their assistance and suggestions for improving the room.

RURAL DISPENSARIES IN BENGAL*

CAUSES OF THEIR UNPOPULARITY AND A PLEA FOR THEIR IMPROVEMENT IN THE SCHEME OF POST-WAR REORGANIZATION OF MEDICAL RELIEF

By B. DAS, M.B., D.T.M., D.P.H.

Health Officer, Dum Dum Municipality and Medical Officer, Dum Dum Municipal Charitable Dispensary

At the end of the year 1940, the total number of rural hospitals and dispensaries stood at 1,681; of these, 16 were state public, 41 state special, 1,242 local and municipal fund (including the village and union board dispensaries), 123 private aided, 71 railway, and 10 subsidized by district boards.

I focus my attention to the 1,365 local, municipal and private dispensaries, most of which are outdoor dispensaries falling under classes III, IV and V of the Dispensary Manual. Taking the rural population as 50 millions (including those of municipalities other than

Calcutta), there is one dispensary for a population of 30,000 in an area of about 40 square miles.

The unpopularity of these dispensaries among the rural population with a high sickness rate may be attributed to the following causes:—

(1) *Inadequate number of dispensaries.*—Not infrequently, the writer had to attend cases of fainting or collapse from the effects of a long and exhausting journey of 10 to 20 miles, taken on foot, by an already debilitated patient. The daily attendance in each rural dispensary often ranges from 100 to 400 patients. The average time that a medical officer can devote for one patient is about 2 minutes or less in the working time of 6 hours a day. It is evident therefore that the patient does not get the time and attention he deserves or desires.

(2) *Inadequate supply of medicine.*—It is a common experience of all medical officers that the average patient thinks that a charitable dispensary gives nothing but 'water' meaning thereby the infinite dilutions of active principles of the drugs. The annual budget for the establishment and supply of medicines in a rural dispensary ranges from Rs. 1,000 to 2,000. The average amount budgeted for the cost of medicines including appliances is from Rs. 300 to 600 per year. As the total annual number stands at 1,500 to 20,000 and the total annual attendances including old and new cases come to about 30,000 to 60,000, the expenditure *per capita* amounts to 1 or 2 annas, and is quite insufficient for the treatment of patients.

The above two factors make the dispensary not an attractive proposition except for those poor and indigent people who can ill afford to buy medicines from a private pharmacy or to call a private doctor.

(3) *The insufficient and in some cases inefficient staff.*—All these dispensaries are in the charge of medical officers of the sub-assistant class with a few exceptions where there are medical graduates. They are of course rendering yeoman's service for the amelioration of the sufferings of a people who form 90 per cent of the population and their aggregate services outweigh those of the better qualified members of the profession, mostly settled in towns, whose services are limited to the upper and middle classes. But the inadequate pay and prospects do not make these dispensaries attractive to the more educated members of the profession who naturally go to and settle at the nearest sadar or sub-divisional towns to build up their private practice. The utilization of more scientific knowledge and experience is thus lost to the rural population who are the backbone of the nation.

The pay of a medical officer in some of the rural dispensaries is as low as Rs. 20 to 30 per month. This is an indirect inducement to the medical officers to do private practice to

*The subject-matter of this paper is a report to the Chairman of the Municipality in reference to a recent Government circular to elicit the views of local bodies, district magistrates and civil surgeons on the causes of present-day unpopularity of rural hospitals with their suggestions for steps to be taken in post-war period to increase their popularity.

Paper abridged by editor.

the detriment of dispensary work. It is no wonder therefore to see him a victim of malicious propaganda and nasty village politics.

(4) *Defective management.*—The management of some of the dispensaries is directly under a local body, either district board or municipality; in some cases it is vested in a local committee, the members of which are rich enough to get themselves treated by private and more popular doctors. It is unusual therefore that they take any interest in the improvement and proper working of these dispensaries. Usually most of them remain on the committee rather for the purpose of self-aggrandisement than for the service of the poor. The government control over these dispensaries is nil or negligible. In many cases the dispensary committee, consisting of laymen, interferes with the professional work of the medical officer who, instead of being free, has to satisfy these members for the security of his service. The public interest of the medical officer thus dwindles into one of job-keeping.

The poor villager thus visits a rural dispensary only because he cannot afford to pay for his medicine and attention. As I have already pointed out, the medical officer cannot treat his patient up to his capacity and satisfaction with an insufficient dispensary stock.

(5) *Want of diagnostic facilities.*—For correct treatment there must be correct diagnosis. On account of the high incidence of diseases such as malaria, kala-azar, dysentery, anæmia and pneumonia, the use of a microscope for examination of blood, urine, stool and sputum is essential in every dispensary, but is not available.

(6) *Obstruction by private practitioners.*—There is a tendency among the private practitioners of a locality to underrate the utility of the services of a charitable dispensary as a part of their propaganda for building up their private practice.

The facts stated above are the results of the experience of a period of 10 years of a medical officer of a charitable dispensary in rural areas. They need serious attention and thought by those of our statesmen and experts who will soon be engaged in the work of post-war reconstruction. I venture to make the following constructive suggestions for consideration in this connection:—

(1) *Area.*—Each dispensary should be a treatment centre for not more than 10,000 people, i.e. the population roughly equivalent to that of one union board.

Site.—As the existing buildings of class III dispensaries with such increase in their number as suggested in (1). The site should be centrally situated and be easily accessible to all sections of people.

The dispensary building should be of masonry work with the following parts:—

(i) Medical officer's room.

(ii) Dispensing room.

(iii) Operation room.

(iv) Room for examination of female patients.

The size of each room should be at least 14 feet \times 10 feet \times 12 feet, and it should be well lighted and ventilated. There should be a verandah on at least three sides, each of at least 5 feet width. The verandahs are to be used by waiting patients, the one for females being partitioned by walls. They should be connected by doors with the medical officer's room. The cost of such a building should not be more than Rs. 2,000 in a post-war period.

(2) *The dispensary budget.*—This should not be less than Rs. 4,000 a year, of which at least Rs. 1,500 should be spent on medicines and appliances, in addition to the cost of quinine and kala-azar specifics which should be distributed free and in a more practical way than at present by the government. The pay of the medical officer should not be less than Rs. 200 per month to attract medical graduates and licentiates alike. It is essential that the medical officer should be provided with free quarters attached to the dispensary.

(3) *The management.*—(a) The whole system of rural medical service should be centralized and the management taken over directly by the government with the civil surgeon of the district as the head of such organization.

(b) The dispensary committee, if essential, should be of the nature of an advisory body with the medical officer as its secretary ex-officio.

(c) The disciplinary control of the medical officer should be the function of the civil surgeon alone.

(d) It is observed that the civil surgeon of the district cannot make time to inspect a dispensary even once a year. It is suggested, therefore, that the civil surgeon should be assisted by an inspecting staff suitably selected and remunerated from among the medical officers of rural dispensaries of not less than 5 years' record of good service.

(e) The Dispensary Manual is old and antiquated and should be rewritten to suit modern conditions.

(4) *Diagnostic facilities.*—Each dispensary should be provided with a microscope with ordinary stains such as Gram's, Leishman, and acid-fast stains. There should be a centrifuge (hand propelled). There should be one sterilizer of the miniature autoclave type for sterilization of dressings, etc. There should be a Berkefeld filter as the water obtainable at such places is very hard for purposes of mixtures. There should be a high-power light of the Petromax type for work at night in emergency cases.

(5) *Efficiency of staff.*—Each medical officer should be required to undergo a refresher course every 5 years to be acquainted with up-to-date developments in diagnosis and treatment. These courses should be arranged in suitable

teaching hospitals. Each medical officer should also have some training in public health.

(6) *Dispensary assistants*.—Each medical officer should have at least one qualified compounder, one dresser, one nurse-midwife or a trained dai, and a peon and one sweeper. Suitable pay and quarters should be provided for these staff.

(7) *Transport facilities*.—Facilities should be provided for removal of patients requiring specialized attention and indoor treatment to sadar, sub-divisional or even Calcutta hospitals. The conveyance charges of such patients should be met from public sources. The sadar and sub-divisional hospitals should be expanded to house such patients.

(8) *Local subscriptions and donations*.—There should be local subscriptions and donations to supplement government funds allotted to the dispensary. The surplus amount should be utilized for expansion of the dispensary service. Two to four indoor beds should be arranged wherever funds permit. They should be used for indigent patients only.

The public health aspect of rural medical service including the maternity and child welfare service cannot be discussed here.

Summary

The actual state of affairs prevailing in rural dispensaries are described by an experienced rural worker. Some suggestions for the improvement in rural medical service in the scheme of post-war reconstruction have been made.

Current Topics

Defeat of Epidemic Typhus

(Abstracted from the *Lancet*, ii, 22nd July, 1944, p. 115)

In the epidemics of the last war, the chief methods of delousing were by heat and to a lesser extent by fumigation. Both these methods have since been improved in various ways by all the principal belligerents. Hot-air treatment has been made more rapid and reliable by the use of air-circulation systems. For fumigation, many alternatives have been proposed instead of the dangerous hydrogen cyanide formerly used—methyl bromide in the U.S.A., methyl-allyl chloride in Britain, trichloroacetonitrile in Germany and methyl formate in Russia. Although hot air and fumigants are effective in killing lice they made little headway in combating general lousiness in a large group of people living under difficult conditions, because the deloused people soon became reinfested. The need has been for some treatment which would keep the lice away, but no suitable insecticide was known which would ensure more than two days' freedom from them. This need for a louse-proofing agent was realized by British scientists early in the war and two partial answers were fairly soon evolved. One was a very finely ground insecticide, 'AL63', which by clinging to dusted underwear protected the wearer from reinfestation for five or six days. The other remedy was to spray the underwear with organic thiocyanates

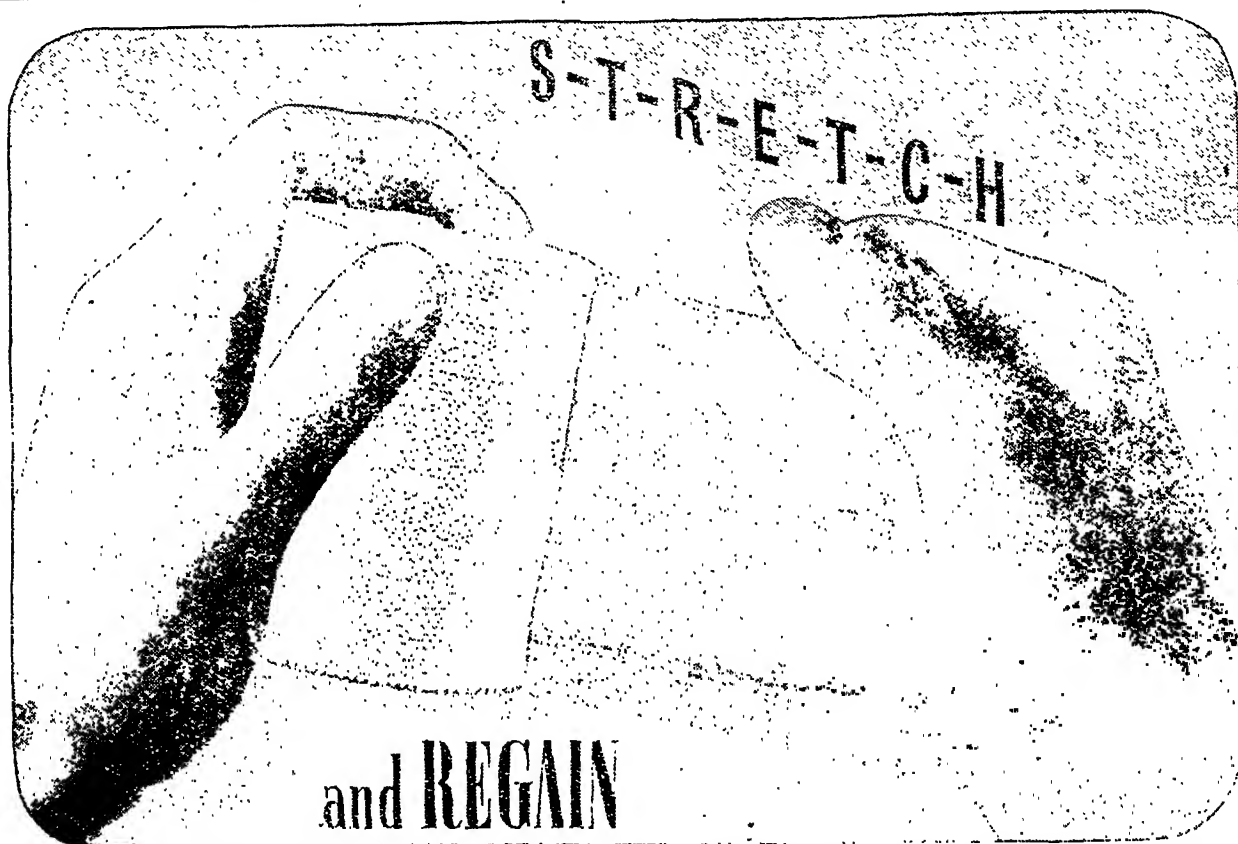
which killed lice and prevented reinfestation for a month. The thiocyanates could also be used on an anti-louse belt woven so as to attract lice which were then killed by the impregnated drug. Unfortunately the thiocyanates caused smarting of the skin if the wearer began to sweat profusely. When the Americans entered the war they set several teams of biologists on investigating the louse problem. Whereas the practical trials in Britain were done on naturally verminous vagrants, the Americans studied the effects of treatments on artificially infested pacifist volunteers. They also acquired much valuable knowledge about the organization of control measures by attempting to eradicate lice from village communities in Mexico. As a result of this work, the insecticide first adopted by the American army was a fine dust, 'MYL', rather like the British 'AL63' but more efficient. This MYL contained pyrethrum which was scarce and wanted for other purposes. In the meantime our Russian allies had developed two synthetic compounds: a powder containing diphenylamine and clothing impregnated with the chemical bis-ethyl-xanthogen. The diphenylamine dust was successfully used among the civilian population in Moscow in the winters of 1941 and 1942. Two large hotels were taken over as treatment centres and the staff instructed in methods of application. The powder is about as insecticidal as AL63. Garments, impregnated with bis-ethyl-xanthogen, which is of the same order of effectiveness as the thiocyanates, were widely worn in Bessarabia when the Russian troops were there last time. The Germans say it has long been used in veterinary practice but that its unpleasant smell makes it unpopular among soldiers.

All these insecticides developed in different countries suffer from more or less serious disadvantages. But the new synthetic compound, 'DDT' (dichlorodiphenyltrichlorethane), seems at last to give trouble-free protection from lice. Synthesized in 1874 by the German chemist Zeidler, its insecticidal properties were not suspected until quite recently. In 1940 the Swiss firm of Geigy & Co. took out patents, and two years later they revealed the formula to Britain and America. Since then intensive research in both countries has perfected its manufacture and use, investigated the health hazard and extended our knowledge of its toxic effects on other pest insects. For combating lousiness it can be used in two principal ways. As a powder diluted with kaolin or pyrophyllite it can be rubbed into underwear and will give protection from lice for two or three weeks. It is even effective when blown up the sleeves or down the necks of dressed people, and was largely applied in that way by the Americans working under General Leon Fox in Naples. The speed of this treatment accounts for his astonishing peak number of 73,000 people treated in one day. Here is obviously the method par excellence for dealing with large-scale lousiness. For people under discipline (soldiers, medical personnel, etc.) it can be used to impregnate under-garments which then protect the wearers from lice for about six weeks. Garments are unaffected and the DDT is not readily removed by laundering. As usually applied it is harmless to the human skin and its smell is unobjectionable. DDT thus provides a simple but effective means of quelling typhus epidemics. Its use demands energy and skill in organization, but now that we at last have the proper tools for the job, plus the experience of the Naples outbreak, it should be impossible for typhus epidemics to ravage territory under Allied control.

Tests of Liver Function

(From the *British Medical Journal*, ii, 16th September, 1944, p. 378)

THERE is a fascination about the measurement of the human functions. Evidence of this is seen in the vast amount of work done on tests of human intelligence, cardiac efficiency, and renal and hepatic function. All this work is inspired by the belief that once we can



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measure a thing and express the result in figures we are at the beginning of science. This is true, however, only if we know just what we are measuring. We have perhaps arrived at that stage in intelligence testing, and have relatively simple tests that can be applied to individuals or groups by a well-trained technician. So far as concerns the kidney, the measurement of the clearance of inulin and diodrast allows us to make legitimate deductions about the rate of filtration through the glomeruli, the renal blood flow, and the work of the tubules; at the same time, however, the tests have become too elaborate and time-consuming for routine use on patients. Neither of these stages has been reached in the measurement of hepatic function, but progress is being made on the road.

Different functions of the liver have in turn attracted attention. Twenty years ago interest was concentrated on the serum bilirubin, and this interest has now been revived by the technical developments associated with the names of Evelyn and Malloy and by the use of bilirubin excretion tests. Nevertheless, the hope that modifications of the van den Bergh reaction would be of value in the differentiation of different forms of liver disease has been generally abandoned. Nowadays we pick our test of liver function according to the object we have in view. If we wish to control a particular hazard in industry or in therapy, as, for example, the risk of liver damage from arsenical treatment, the serial repetition of a single test such as the serum bilirubin or the hippuric acid synthesis may be adequate. In the differential diagnosis of a case of jaundice, and more particularly the decision whether it is due to obstruction in the outflow of bile or damage to the parenchyma, it is desirable to apply a battery of tests. In an article in this *Journal* MacLagan recommends the colloidal gold and the phosphatase tests, followed if necessary by the galactose tolerance. Although experience with grouped tests in this country has shown the help they can give in diagnosis, their limitations must be realized. American workers have had an opportunity to use them on a large scale during the recent outbreak of hepatitis after yellow fever vaccine. In many of the more protracted cases there was no evidence of disturbance of any function of the liver except the excretion of bile. Presumably the damaged cells had regenerated, but adequate connections had not yet been re-established between the lobule and the portal tract. It would be misleading to call this condition obstructive jaundice in the ordinary sense. Finally, the clinician may wish to exclude hepatic disease in the investigation of ill health, and Higgins and co-workers have shown that chronic disease of the liver is unlikely to be present if the serum bilirubin and the plasma proteins are normal.

All this is empirical, and the clinical scientist will ask how the tests help him in understanding the morbid physiology of hepatic disease. To what extent are the different tests correlated together? Is a high phosphatase value due to the disturbance in the absorption of calcium because the bile is not flowing into the intestine, or is it due to a disturbance in the synthesis of glycogen, which occurs by a process of phosphorylation? Correlations of this kind have not yet been worked out, but we do appreciate the relation between the liver and serum proteins. The serum proteins undergo quantitative and qualitative alteration when the liver is diseased, and the results are every bit as important as in nephritis. In chronic liver disease, notably cirrhosis of the liver, the serum albumin is generally reduced, whereas the serum globulin is normal or increased. The degree of reduction in the level of serum albumin seems to be correlated with the prognosis as to the duration of life, with the clinical course of the disease, and with the appearance and disappearance of ascites. There is apparently a defect in the synthesis of serum albumin, and though these patients are able to absorb and retain protein, they are unable to convert it into serum albumin. In acute hepatitis the change in the serum proteins is more of a qualitative than a quantitative nature, and it may be

better demonstrated by one of the flocculation tests than by the simple chemical analysis of the serum proteins. There is a shift to the right in the protein pattern with an increase in the gamma globulin. At present we do not understand why changes in the serum globulin occur in disease of the liver, though it seems as if the increase in the largest molecular weight protein, the gamma globulin, is an effort to compensate for the decrease in the smallest molecular weight protein, the albumin.

Laboratory Tests in the Diagnosis of Liver Disease

By N. F. MACLAGAN, M.D., M.Sc., M.R.C.P.

(Abstracted from the *British Medical Journal*, ii, 16th September, 1944, p. 363)

THE clinical value of laboratory tests in the diagnosis of liver disease has been reviewed with special reference to the serum colloidal gold reaction (319 cases), the serum alkaline phosphatase (136 cases), and the galactose index (145 cases).

The first two tests, taken together, often give valuable diagnostic information when considered in conjunction with clinical data. A jaundiced patient with a negative gold reaction and a phosphatase above 35 King-Armstrong units probably has biliary obstruction; one with a positive gold reaction and a phosphatase below 25 units probably has not. A 4 or 5 + gold reaction is against biliary obstruction whatever the phosphatase level.

The galactose index is useful as a confirmatory test in special cases and for assessing the degree of liver damage when present. It is also of value in the diagnosis of hyperthyroidism.

The results given indicate that out of 100 jaundiced patients the distinction between biliary obstruction and generalized liver disease could be made in 75 cases with the gold and phosphatase tests, and in a still higher proportion if the galactose index was included.

Investigations in the Chemotherapy of Malaria in West Africa

I.—Treatment with Quinine and Mepacrine

By G. M. FINDLAY

and

OTHERS

(Abstracted from the *Annals of Tropical Medicine and Parasitology*, Vol. XXXVIII, 30th September, 1944, p. 139)

IN the treatment of *Plasmodium falciparum* infections in Europeans in West Africa by quinine alone, by quinine and mepacrine, or by mepacrine alone it was found that mepacrine alone, is as satisfactory as quinine alone or quinine and mepacrine, provided that an initial dose of 0.8 gm. mepacrine is given during the first 24 hours of treatment.

Small doses of mepacrine, 0.3 gm. daily, are capable of dealing with small numbers of parasites in the peripheral blood stream, but with larger parasite counts larger initial doses of mepacrine are required.

A low initial parasite count may be followed by a considerable rise in the number of parasites in the peripheral blood stream.

No toxic results followed the larger doses of mepacrine, despite the fact that some of the patients had been taking 0.6 gm. mepacrine weekly as a suppressive for six months or more.

The 'return' rate of patients treated with mepacrine and quinine or mepacrine alone is shown to be 26.6 per cent; but it is not possible to determine whether such return cases are relapses or reinfections.

It is considered that in the treatment of uncomplicated cases of malignant tertian malaria in Europeans in West Africa—and such uncomplicated cases constitute the great majority in persons who have been taking a malarial suppressive drug with regularity—quinine can be entirely replaced by mepacrine.

Vi Agglutinative Properties for *Bacterium typhosum* demonstrated following Infection with Malarial Parasites

By M. B. COLEMAN

(Abstracted from the *Journal of Laboratory and Clinical Medicine*, Vol. XXIX, September 1944, p. 916)

Vi agglutinative properties were demonstrated with typhoid bacilli in significant dilutions of sera from: (1) twenty-three of thirty-four patients having neurosyphilis or latent syphilis and who were receiving malarial therapy; (2) two of ninety-six individuals who had received no malarial therapy; (3) eleven of twenty-eight patients with clinical malaria; and (4) fourteen of thirty-one neurosyphilitic patients who had been treated by intravenous injection of typhoid vaccine.

Two hypotheses are offered: (1) that malaria parasites possess Vi antigen, and (2) that latent agglutinative properties should be considered in evaluating these observations should be considered in evaluating Vi agglutination. A continuation of the study should include the examination of various species of bacteria for Vi antigen and the determination of factors that may stimulate latent Vi agglutinative properties.

Clinical Observations on Dengue Fever Report on 100 Cases

By MAJOR JOSEPH S. DIASIO
and

CAPTAIN FRED MACD. RICHARDSON

(Abstracted from the *Military Surgeon*, Vol. XCIV, June 1944, p. 365)

SINCE symptoms and signs of dengue are notoriously variable, even within the limits of a single epidemic, we have reported as percentages the outstanding symptoms and signs, and a detailed analysis of our observation has been made under the appropriate headings.

Analysis of symptoms.—The onset of the disease in the typical patient was so sudden that the patient could name its hour; in a few cases even the minute. The usual symptoms were severe headache, frontal or occipital, accompanied by lumbar backache and supra-orbital pain. Almost invariably there was anorexia and either or both loss of taste and bitter taste. Chills with rapidly rising fever were frequent, and patients often reported nasal symptoms suggestive of acute coryza, or a mild, fleeting sore throat. Joint pains were prominent, knees and shoulders being most frequently affected. Nausea and abdominal cramps were occasional complaints. Insomnia, characterized by drowsiness and restless, disturbed sleep, was nearly universal.

Headache.—Ninety-four per cent of patients complained of headache, usually characterized by them as 'splitting'. Often the first noted symptom, headache, in the majority of cases, was frontal or supra-orbital, but in roughly one-third of the series was occipital or parietal. Sudden movements of the head intensified the pain.

Backache.—Eighty-nine per cent of the patients complained of backache, usually a dull 'grippy' pain which

was most intense across the lumbar region and in the flanks, but in a few cases extended along the whole length of the spinal column. The ache seemed to be fairly definitely in the spinal muscle mass, probably in the inter-vertebral ligaments. It was intensified by motion, tended to be minimized by quiet and in some cases was accentuated by pressure on the muscles of the back. Similar in type to this backache were pains variously named by the patients as 'leg ache', 'knee ache', or 'pains in the joints'. These pains were myalgia-like, noted along the hamstring muscles and in the regions of tendon insertions about the joints. Most commonly affected were the knee joints, less frequently the shoulder, elbow and ankle. A few of the patients complained of pain and stiffness in the hands. These leg or joint pains were seen in seventy-five per cent of the series. Fourteen of the patients complained of stiffness of the neck as distinct from backache.

The other, and clinically more characteristic, painful complaint is that of ocular soreness. This pain often is not noted by the patient until four to twelve hours after the acute onset of the symptom complex and is often described as a 'burning ache', in milder cases as 'tiredness' of the eyes. It seems not to be located in the eyeball itself but rather to be in the orbital muscles and is intensified by use of these muscles. Seventy-four per cent of the series exhibited this complaint. A few reported mild but disturbing photophobia.

Chilly sensations, more severe than those seen in la grippe but still not the shaking rigors of malaria, were described by fifty-four of the patients. These were described usually within the first twelve hours, in only fourteen did they usher in the disease.

Predominant among symptoms were those connected with appetite and taste. Eighty-five per cent of the patients complained of anorexia. It usually succeeded the onset of symptoms, in a few cases it preceded, in no case did it precede by more than twelve hours. This anorexia did not appear to parallel the severity of other symptoms, being quite apparent in patients with an otherwise mild illness and completely absent in several with severe symptoms and high fever. Loss of taste and/or the consciousness of a 'brassy' taste in the mouth frequently were associated with the anorexia. The former symptom was present in fifty-five, the latter in forty-five per cent of the series. In the majority these two symptoms were linked, usually accompanying the loss of appetite.

Insomnia, characterized by sleep that was restless and frequently interrupted by dreams, was noted in fifty-three per cent. It was curious that several patients who noted their first symptoms on awakening had had a good previous night's sleep, while their succeeding night's sleep was poor. Several whose symptom onset was in the evening, were immediately the victims of disturbed sleep.

Twenty-nine patients mentioned 'weakness', usually of the legs, occasionally a generalized feeling, as an early symptom. In fact, in nearly every case in which weakness was a complaint it was the first noted symptom. Dizziness constantly accompanied the weakness, and four of our patients suffered syncopal attacks before admission. Constipation, regarded by other authors as nearly universal, was seen infrequently in our patients.

Interesting, as a point in differential diagnosis, was coryza. Twenty-four patients of the series remembered a feeling as of a fresh cold with definite stuffiness of the nose and some coryza. In most of these cases this feeling was noted between a half and a full day before the dengue symptoms made themselves felt, in no case of dengue did the symptoms persist beyond the onset of the disease. This was one of the main early differential points between dengue and rubella. Of the series, twelve had a fleeting sore throat with the same time distribution as the coryzal symptoms.

Within forty-eight to seventy-two hours of the onset of symptoms, most of the patients showed a return of temperature nearly or quite to normal. At the same time appetite returned, pains ameliorated, the rash

lessened and the patient felt quite well. This phase lasted usually about two days and was followed by a sudden return of fever resembling, but slightly less severe than the primary episode. At this time the head and backache and the ocular pains recurred and the rash again became evident. The second period of fever was shorter than the first, and, with the final return of the temperature to normal, about twenty per cent of our patients complained of itching affecting the palms of the hands, the wrists, the soles of the feet and the lower legs. Eleven of our patients who had failed to show rash on admission, exhibited typical exanthemata with the febrile recurrence. The recurrent symptoms were less severe than at the time of their primary manifestations. This experience was not in accord with textbook descriptions.

ANALYSIS OF PHYSICAL SIGNS

Sclerae.—The most characteristic early physical sign of dengue is, in our opinion, scleral injection. This injection varied from a vague, slightly abnormal increase of the vessels to a dense, diffuse, inflammatory change. In three cases presenting urticaria from the onset of symptoms, there was a mild conjunctival chemosis. Scleral changes were observed in eighty-nine per cent of our series and did not always parallel the disease in severity, i.e. a few of the most severely ill had the mildest of eye signs, while some whose eyes resembled 'holes burned in a blanket' were numbered among the milder cases. There was also present a diffuse eyeball tenderness, accentuated by pressure, in about one-half of those with scleral injection. The injection did not tend to recur with the secondary temperature rise but seemed to pass steadily, if somewhat slowly, toward recovery, and was largely normal by the fifth day of the illness.

Injection of the free edge of the posterior palate was seen in seventeen per cent, and of the posterior wall of the oropharynx, in the same number of cases. The injection was not coincidental in all cases. No record was kept of coincidental incidence but it is our impression that it occurred in about sixty per cent of the fraction, or in ten cases. It was similar to that seen with any catarrhal inflammation of the oropharynx and was not attended by angina simplex.

Completely different from the above mentioned palatal and pharyngeal injection was an enanthem which was noted in fifty-seven per cent of the series. We have found no description of this rash in our textbooks and so thought it worth while describing minutely. Early, usually within the first twelve hours, a few pin-point sized, discrete, glistening vesicles may be seen on the posterior half of the soft palate. They are surrounded by no areola, and are easily missed. In the succeeding twenty-four hours there develops beneath these minute vesicles a star-shaped area of redness which gradually enlarges as the vesicle disappears, reaching, somewhere in the second or third day of the disease, a pin-head size, a discrete distribution and a morbilliform character. It closely resembles the mucous membrane rash of rubella. This enanthem gradually fades during the period of intermission and does not recur with the exanthem at the time of the secondary febrile rise.

The exanthem seen in our patients exhibited certain differences from the textbook descriptions. Indeed, it was these differences that first decided us to make this survey. The primary difference was that on admission, seventy-nine of our cases showed a typical morbilliform rash which, in the literature, was described as occurring at the period of recrudescence. This rash, when present, was variable in severity and distribution. In the mild cases the rash consisted of a few discrete, light-pink, morbilliform spots found most often on the sides of the thorax, the inner surfaces of the upper arms and in the lumbar region. The severe case showed unbroken erythematous areas covering the face below the forehead, the neck, the shoulders and the thorax, with the typical morbilliform character becoming apparent at the edges of the confluent areas, notably the lower one-half of the upper arm, the upper part of the abdomen and the thoracic extensions of the axillary spaces. The

rash, whether mild or severe at the onset, proceeded through parallel developmental stages, i.e. it faded somewhat (but not completely) during the remission, only to recur during the period of recrudescence. In most of the severe cases the rash was less intense at its second appearance. Three of our cases showed a rather marked urticarial reaction at the onset of symptoms. Each of these patients had a history of previous urticaria.

Thirty-three of our cases showed facies described as typical, at the onset. Here the entire countenance was flushed and swollen and the lips were dry. The only differential point, between this 'flushed-face' and the severe rash affecting the face, was the swelling of the lips, the cheeks and around the eyes, and we have arbitrarily divided our classification on this difference. It was further noted that, with the recrudescence, this flush did not reappear while the rash did.

Coating of the tongue was seen in fifty-three patients. This coating varied from a light whitish film to a heavy, yellowish, furry coating, seemingly *pari passu* with the general severity of symptoms, being lighter in mild cases and heavier in the more severe. It disappeared during the remission and did not recur. Concurrently with its disappearance, taste and appetite largely returned.

Adenitis was a constant feature of the disease; in fact, it was so constant that in its absence we did not diagnose dengue. The nodes affected were in three groups; posterior cervical, epitrochlear and inguinal. They were uniformly of shotty consistency, usually non-tender, bilateral, and with a tendency to occur in chains rather than singly. The occurrence of adenopathy in the posterior cervical region was ninety-four per cent, in the epitrochlears ninety per cent, and in the inguinal region in eighty per cent of the series. It lasted through the period of recrudescence, being present, but less apparent, at the time of discharge of the greater number of the patients.

Temperature curves were found to be of two types, namely, typical saddle-back in fifty-five cases, and non-saddle-back in forty-five cases. The latter were further divided into thirty-three with the temperature return to normal by lysis following the initial rise, and twelve which were unclassified.

In the first type (the saddle-back) admission times of the patients varied from thirty minutes to seventy-two hours from the time of onset of the original symptoms. The initial temperatures on admission varied from 99.2°F. to 104°F. No correlation was noted between the time after onset and the height of the admission temperature. The secondary rise occurred from three to six days after the onset of the symptoms, the majority on the fourth and fifth days. The last temperature before the rise varied from 97.2°F. to 100°F. and at the top of the rise, ranged from 98.6°F. to 103.4°F. The only noted correlation was that many of the patients with high initial temperatures did not return to normal during the intermission, and exhibited higher excursions during the secondary rise than did those with lower initial temperatures. The pulse rates generally were comparatively slow during the later stages of the initial fever and during the remission period, but at no time was extreme bradycardia observed. Attempts at averaging temperatures failed to show characteristic curves and, for that reason, typical temperature charts of the saddle-back and non-saddle-back varieties are presented.

Of the non-saddle-back type of temperature curve, twelve cases presented curves that defied classification within the confines of any one group, and so were grouped together. The clinical course of these patients presented no constant differences from that of patients within the other two great groups and we have no explanation for their aberrant behaviour as regards temperature; any more than we have a reason for one group to show a typical saddle-back curve and another, under basic conditions exactly similar, to show a curve which after the initial rise, returns to normal by lysis.

The remaining thirty-three patients, in no way differing symptomatically or physically from the rest of the

series, showed a completely different type of temperature curve. The admission time of this group varied from two to sixty hours from the time of onset of symptoms; and the initial admission temperatures varied between 99.6°F. and 104.9°F. Here again there was no correlation between the height of the fever and the time interval from the onset of the symptoms. Nine of these thirty-three patients showed a temperature curve in which there was a plateau somewhere in the first three days. Following this period, their temperature return to normal was in no way different from the twenty-four who had no plateau in the curve. In the entire group, the temperature return to a constant normal occurred in from two to seven days after the beginning of symptoms, with the greatest number showing the return on the fourth day. In none was there any semblance of a secondary rise with a saddle-back temperature curve. Temperature curves of this type, previously seen in dengue, are described by Stitt.

ANALYSIS OF LABORATORY FINDINGS

An occasional patient exhibited a moderate albuminuria during the course of the febrile stages, but with the return of temperatures to normal, the albumin disappeared from the urine.

No patients showed changes in hæmoglobin levels, or in the total number of red blood cells, that could be attributed to dengue.

Leucocyte counts were made on admission to the hospital on all patients, and again immediately following the secondary temperature rise. On patients who did not exhibit a saddle-back temperature curve, the counts were made on the fifth day of the disease. Total leucocyte counts on admission averaged for the series, 5,450; the range was from 10,000 to 3,600. An average of the counts made on the fifth day, or the day following the secondary rise, was 3,500; with the variation between 5,600 and 2,500. It is interesting to note that, on all patients admitted during the first twenty-four hours of the disease, the leucocytes were well above the average, ranging between 10,600 and 5,600. The low average of admission counts was due to the greater number of second and third day admissions among the patients.

Reduction in the polymorphonuclear elements, of from ten to twenty per cent below normal, was found to be present in the second series of counts.

The average stay in hospital was 7.47 days per patient.

Due to frequent changes in troop locations, no systematic follow-up of patients was possible, but about ten per cent of the series, accidentally encountered at later dates, confessed, without exception, to a period of from seven to ten days following discharge from the hospital, during which a constant physical weakness was observed, and in which any effort was abnormally fatiguing. There were no other sequelæ noted in the series, or in any of the other patients, outside the series, who were under treatment.

Neurological Complications of Relapsing Fever

By R. B. SCOTT

(Abstracted from the *Lancet*, ii, 30th September, 1944, p. 436)

THE campaigns in the Libyan Desert yielded cases of relapsing fever of a type not previously known in Egypt. They were due to infection with a strain of *Treponema recurrentis*, whose immunological characteristics have not yet been determined, transmitted by the bite of an unnamed argasid tick of the genus *ornithodoros*, bearing a close resemblance to *O. erraticus*, the vector of the Tunician strain of treponema. This tick probably inhabited the burrows of desert rodents and infection was commonly acquired in caves, slit trenches and tombs.

Characteristic of this fever was the high proportion of cases in which the central nervous system was

invaded. Most descriptions of the disease include the comment that nervous sequelæ occur and that they are more common in the tick-borne than in the louse-borne fever; but their frequency and variety are not generally recognized. This paper is concerned with a small series of such cases seen in 1941 and 1942; its observations consequently apply to the disease of the north-west African coast. It is likely, however, that this reservation is not absolute: the characteristic of *Tr. recurrentis* are so liable that strains from the same locality, and even from different relapses in the same case, may show immunological variations. Thus the clinician is probably justified in discounting the importance of differences of strain and the regarding tick-borne relapsing fever as an entity, however, heretical the immunologist may consider this view.

Neurological complications occurred in 9 of 41 cases of tick-borne relapsing fever acquired in the Western Desert. They arose at various times in the illness but were more common after the third week.

The case fell into three categories: (1) those with meningitis, (2) those with signs of focal nervous damage, and (3) those combining the features of the first two groups.

The cerebrospinal fluid showed a lymphocytic pleocytosis with a total cell count sometimes as high as 2,000 per c.mm.

Treatment with arsphenamine was ineffective.

The prognosis was hard to assess: some cases showed repeated relapses but the majority recovered completely. There are no deaths.

Dangers of Intensive Alkali Treatment in Blackwater Fever

By B. G. MAEGRAITH

and

R. E. HAVARD

(Abstracted from the *Lancet*, ii, 9th September, 1944, p. 338)

THE intensive alkali treatment of blackwater fever is dangerous, and the reasons for its introduction were unsound.

The mortality of blackwater fever has not diminished since intensive alkali treatment was introduced.

The administration of alkali in blackwater fever should be limited, and where possible, controlled by estimation of the alkali reserve.

Hepatitis after Yellow Fever Inoculation Relation to Infective Hepatitis

By G. M. FINDLAY

and

OTHERS

I. CLINICAL AND PATHOLOGICAL FINDINGS

(Abstracted from the *Lancet*, ii, 9th September, 1944, p. 340)

THE clinical symptoms are analysed in an outbreak of hepatitis following the injection of icterogenic yellow fever vaccine.

The latent period varied from 26 to 239 days, with an average of 101.5 days. One fatal case occurred among 689 patients; the lesions in the liver were those of subacute hepatic necrosis.

No difference could be detected between the clinical and pathological findings in post-inoculation jaundice and infective hepatitis.

Hepatitis after Yellow Fever Inoculation Relation to Infective Hepatitis

By G. M. FINDLAY,
and
OTHERS

II. IMMUNOLOGY AND EPIDEMIOLOGY

(Abstracted from the *Lancet*, ii, 16th September, 1944, p. 365)

POSSIBLE examples of spread of post-inoculation jaundice to contacts who had not been inoculated with heterogenic yellow fever vaccine are reported.

The incidence of infective hepatitis in childhood and adolescence in a sample of British troops has been ascertained. From this, evidence has been deduced that a previous attack of infective hepatitis gives a certain measure of protection against an attack of post-inoculation jaundice, though the protection is not absolute.

A complement-fixation test has been developed, the results of which tend to show that there is an antigenic relationship between the agents responsible for infective hepatitis and post-inoculation jaundice.

Efforts to transmit post-inoculation jaundice to man and various animals are described.

A comparison is made of infective hepatitis and post-inoculation jaundice; the conclusion is reached that they are due to the same or to very closely allied agents.

Amoebiasis of the Uterus

By DAMASO DE RIVAS

(From the *American Journal of Tropical Medicine*, Vol. XXIV, May 1944, p. 185)

AMOEBIASIS is the term commonly used to indicate an infection of the body by unicellular organisms known as amoebas. These parasites of which several species have been described, commonly are found in the gastro-intestinal tract where they may give rise to pathological changes. Of special clinical importance is *Endamoeba histolytica* which commonly invades the large intestine and is the cause of amoebic dysentery also called tropical dysentery or intestinal amoebiasis. This parasite may also directly invade the lower part of the ileum and appendix and cause appendicitis and by metastasis may be carried to the liver and lungs and give rise to amoebic abscesses in these organs.

The case to be reported is that of a woman, M. B., aged 70 years, who was in a hospital for mental disease as a senile case for about four years, she never was out of the country. The blood showed a rather marked degree of secondary anaemia, pernicious in type. Before her death, 27th October, 1942, she had intermittent attacks of diarrhoea for about six weeks, the faeces were not examined for parasites.

There was nothing of importance in the physical history of the case that would have had any definite bearing on the cause of death except that the physician in charge of the case, noticing a rather profuse vaginal discharge, on examination found the uterus enlarged, the cervix swollen, soft and ulcerated and cancer was suspected.

At the autopsy I did not find any pathologic changes of importance to account for the immediate cause of death beyond a generalized arteriosclerosis, senile changes of the internal organs and a moderate degree of hypostatic pneumonia. Next in importance was the examination of the uterus for the evidence of cancer.

Macroscopically the uterus was found moderately enlarged and soft. The cervix was swollen, soft, eroded and ulcerated and showed several small hemorrhagic areas. Microscopical examination of the sections showed a subacute ulcerative inflammation, congestion, sero-cellular infiltration and granulation tissue, no evidence of a neoplastic growth was found. On further examination, however, quite unexpectedly and to my surprise, I detected several round and oval bodies in the submucosa below the ulcers and also into the deeper

layers of the tissues. A more detailed study of the sections revealed these bodies to be the vegetative form of *Endamoeba histolytica*.

Laboratory and Clinical Trials of Patulin

By J. M. STANSFELD
and
OTHERS

(Abstracted from the *Lancet*, ii, 16th September, 1944, p. 370)

PATULIN is bacteriostatic against a wide range of Gram-positive and Gram-negative bacteria. Its bacteriostatic activity is materially reduced by preliminary incubation at 37°C. overnight of dilutions in broth at pH 7.4, or by the addition of horse serum. It is stable in solution at pH 6.0 for several months at room temperature.

Toxicity experiments in mice have shown a relatively small margin between concentrations which kill the animals and those which produce bacteriostasis *in vitro*. Lethal and toxic effects are more readily produced by subcutaneous or intraperitoneal inoculation than by intravenous injection. Two experiments in mice resulted in failure to cure infections with influenza virus A or with *Bact. typhosum*.

Controlled clinical trials in the treatment of the common cold with patulin have shown no advantage from the use of this substance as compared with the use of a control buffer solution without patulin, nor did patulin appear to be of value in the treatment of human cases of conjunctivitis.

These therapeutic trials emphasized the great difficulty of assessing the effect of treatment in view of the lack of real objective signs which, in the common cold, can serve as a check of the patient's subjective feelings. A serious attempt was made in the main trial of 100 cases to eliminate personal bias, both during treatment and in recording results. Neither investigator nor patient knew whether patulin or control solution had been used for treatment, and all results were obtained before any analysis was begun.

The main trial was carried out on 100 men at a recruit establishment during the season of autumn colds. Patulin was given to 50 and the control solution to 50. The treated and the control groups were comparable as regards age, symptomatology, duration of the cold before and after treatment, and the bacteriological findings. Neither the control nor the patulin solution appeared to produce any effects which could be described as either immediate or dramatic.

The actual solutions used in the final series of trials were tested for bacteriostatic power 9 weeks after preparation and after the conclusion of the trials. When compared with a freshly prepared solution it was found that they retained full activity.

It had to be concluded that patulin had no demonstrable effect on the course of this series of colds as compared with the natural evolution of the disease.

Penicillin for Civilians

(From the *British Medical Journal*, ii, 2nd September, 1944, p. 317)

THE following brief memorandum on the selection of cases for treatment with penicillin under the arrangements for civilians noted in these columns on 19th August (p. 250) has been issued by the Ministry of Health.

The list of diseases for which penicillin may be used is as follows:—

1. Conditions which should be admitted to hospital if the case is otherwise suitable for treatment with penicillin:

Staphylococcal infections.—Septicæmia. Early acute osteomyelitis. Severe carbuncle, cavernous sinus thrombosis, or any other life-endangering infection.

Hæmolytic streptococcal, pneumococcal and meningococcal infections.—Any life-endangering infection (septicæmia, pneumonia, meningitis) which has failed to respond to adequate sulphonamide treatment.

Gas gangrene

2. Conditions deserving special consideration, which may be treated if supplies are sufficient: (a) Injuries of the eye and infections of the conjunctiva and cornea. (b) Sepsis in wounds and burns. (c) Infections of the skin resistant to other forms of treatment (syccosis, impetigo, etc.). (d) Sulphonamide resistant gonorrhœa. (e) Acute empyema and pyogenic infections of the pleura as a complication of tuberculosis. (f) Traumatic lesions, including compound fractures of any bone, extensive muscle injuries, facial injuries, injuries necessitating suture of tendon or nerve, thoracic injuries (hæmothorax), and post-traumatic pneumonias.

If supplies are sufficient, approved departments and hospitals specializing in ophthalmology, neurosurgery, thoracic surgery, burns, etc., may be given a supply of penicillin.

3. Conditions which will not be treated are those caused by organisms not known to be susceptible to penicillin (including rheumatic fever, ulcerative colitis, and all other intestinal infections). Bacterial endocarditis and syphilis will also be excluded.

Clinical Trial of Patulin in the Common Cold

(Abstracted from the *Lancet*, ii, 16th September, 1944, p. 373)

IN a large clinical trial of patulin in widely distributed areas in Great Britain and lasting from the beginning of December 1943, to the middle of April 1944, no evidence was found that patulin is effective in the treatment of the common cold.

The Rh Factor in Feeble-mindedness

(From the *Journal of the American Medical Association*, Vol. CXXV, 26th August, 1944, p. 1193)

THE importance of the Rh factor in foetal erythroblastosis and in unfavourable reactions in transfusion under certain circumstances is well established. The Rh factor in the blood of a foetus where the father is Rh positive can lead to the production of antibodies in an Rh negative mother, which in turn can destroy red corpuscles in the foetus leading to foetal anæmia and its consequences. Now a beginning has been made in the study of the possible relationship of the Rh factor to mental deficiency. Yannet and Lieberman found that, in the case of 53 children with mongolism, birth trauma and other specific types of feeble-mindedness, the distribution of the mothers as to Rh positive and Rh negative corresponded closely to the accepted normal white average in the United States. In the case of 56 children with mental deficiencies of unclassified nature, however, 14 of the mothers were Rh negative, which is more than twice the average for the general population. Of these 14 Rh negative mothers 11 had Rh positive children. While the number of cases in this series is too small to have any statistical significance, further study on a much larger scale of the Rh factor in feeble-mindedness seems advisable. Commenting on the work of Yannet and Lieberman, Cook points out that destruction of foetal blood cells by anti-Rh bodies in the blood of mothers may lead to serious injury to the foetal brain from anoxia, possibly also in other ways. In foetal erythroblastosis and icterus, degenerative changes in cerebral structures (kernicterus) may occur on a large scale. The idea that the Rh factor may play a rôle in feeble-mindedness turns the attention to the possibility of preventing its disastrous effects. It has been suggested that tests

of the blood for anti-Rh agglutinins in pregnant Rh negative women may give warning of the danger of foetal erythroblastosis and thus facilitate appropriate treatment immediately after birth. Further developments of great interest in the understanding of the Rh factor and its effects are foreseen.

Observations on the Toxicity of Stilbamidine

By R. KIRK

and

A. J. HENRY

(Abstracted from the *Annals of Tropical Medicine and Parasitology*, Vol. XXXVIII, 30th September, 1944, p. 99)

1. THE immediate reactions produced in man by intravenous injection of the diamidines are summarized and discussed.

2. An account is given of certain late toxic effects which occurred in cases of kala-azar treated with solutions of stilbamidine which were not freshly prepared.

3. Evidence is given that these late toxic effects were not due to stilbamidine *per se*, but resulted because the solution with which the patients were injected contained also other substances which have been shown to be more toxic for mice than is stilbamidine.

4. The chemical changes which may occur in solutions of stilbamidine are described.

5. Some observations bearing on the fate of stilbamidine after intravenous injections into the human subject are recorded and their significance in relation to dosage and methods of administration of the drug is discussed.

Technique of Lumbar Puncture

(From the *Lancet*, ii, 23rd September, 1944, p. 410)

THERE is need for better teaching of the minutiae of lumbar puncture. Most beginners without much practical instruction, can perform the little operation after a fashion, but even experienced operators commonly fall into error through faulty technique, producing needless distress to the patient, a blood-stained fluid relatively worthless for diagnosis, or avoidable trauma to the surrounding parts. There have been suggestions indeed that lumbar puncture can cause herniation of the nucleus pulposus. That the needle does sometimes penetrate the intervertebral disc is demonstrated by Carnegie Dickson's report of cartilage cells in specimens of fluid sent for examination; he also found myelocytes and nucleated red cells from the bone marrow, due to penetration of the vertebral bodies. Damage to the intervertebral discs almost certainly accounted for the back pain following lumbar puncture in 35 cases of meningitis reported by Billington. Munro and Harding, at the Boston City Hospital, made an x-ray study of needles in position for two-needle myelography. Flexion of the spine was not adopted in these patients, for Munro holds that this position does not secure more room for the needle between the adjoining bones. Of 50 needles studied, 36 were in such a position that if they had been pushed an average distance of 4-5 mm. further in the same line they would have penetrated the annulus fibrosus—one needle was within 2 mm. of it. Another example of avoidable trauma is damage to the roots of the cauda equina, an accident that may happen when persistent but incautious efforts are made to strike fluid in difficult cases, particularly when an unnecessary large needle is used; it may leave a permanent dropped foot. The most serious accident of lumbar puncture is the introduction of infection, leading to septic meningitis. Wet sterilization of the needle is often to blame.

The technique, then, must be thoroughly learnt and as carefully followed. The needle should be chosen for the particular job. For unanesthetized patients likely to make sudden jerks, such as those with purulent meningitis, a nickel needle is best because it will bend rather than break. For quiet patients a steel needle is preferable because it can be made sharper and used in finer sizes. It should be of suitable length, 2 inches for infants, $3\frac{1}{2}$ inches for stout adults, and of suitable diameter, gauge 20 in steel for general use, gauge 22 in steel for infants, gauge 17 or 18 in nickel for violent cases. For outpatients the Dattner needle is ideal. It consists of an extremely fine inner needle carried in a larger one. The outer penetrates as far as the deep aspect of the ligamentum subflavum, whence the fine needle is pushed forward to make a minute puncture of the theca. Needle points should be sharpened frequently and their sharpness checked with a lens before use. Both needle and manometer should be dry-sterilized. The operator should have a clear idea of the approximate depth at which fluid will be struck; this varies from $\frac{3}{8}$ inch in a small infant to over 3 inches in some adults. The passage of the needle should be under perfect control at every stage, the operator's hand being steadied by pressure on the patient's body. The patient should lie on a solid table rather than a bed, with the plane of the back exactly vertical, and most operators employ the fully flexed position. Strict asepsis is required, but face-mask and gloves are not essential provided the operator does not allow his fingers to stray over any part of the needle shaft which may penetrate the skin. The operator should be seated. The third lumbar space, which lies at the level of the iliac crests, or the fourth, is usually employed. In difficult cases the sitting position is sometimes successful, but it cannot be used when the fluid pressure has to be measured. The local anæsthetic is injected only intradermally and subcutaneously, or as far as the interspinous ligament when a gauge 20 or finer needle is used.

The skin is pierced with the sharpened point by rolling the butt of the needle between finger and thumb. The needle is inserted exactly in the midline, in a plane exactly at right angles to the plane of the back, and with a slant towards the head corresponding to the slope of the vertebral spines. It should be felt to pass through the interspinous ligament and down to the level of the root of the adjacent vertebral spines. Here it may encounter bony obstruction, and at this point the assistant forcibly draws up the patient's knees as near as possible to his chin, thus opening the 'gate' between the vertebral rings. The needle should now be felt to pass through the ligamentum subflavum. From this point until fluid is struck the stylette should be removed every two millimetres. The practised operator will usually be able to feel the puncture of the dura and sometimes, immediately thereafter, of the arachnoid. Reid and Carnegie Dickson advise inserting the needle with the bevel edge in the spinal axis so that as it pierces the dura it merely separates and does not cut across the main fibres, which run longitudinally. The small opening thus caused closes again as soon as the needle is withdrawn, whereas when the bevel cuts across the longitudinal fibres a small hole is made through which fluid continues to escape, causing low-pressure headache. On no account must the needle be pushed right through the theca to injure the anterior venous plexus, the commonest cause of a blood-stained fluid and one that is avoidable in a quiet patient. If the fluid is not obtained, although the needle appears to be in the correct position, it should be withdrawn to skin level, the position of the patient checked and a fresh start made. The pressure of the fluid cannot be estimated, except in extreme cases, by the rate at which it escapes from the end of the needle. The manometer must be attached to the needle before even 1 c.cm. of fluid has escaped, and, before taking a reading, the patient must be completely relaxed with head and legs extended slightly until he is quite comfortable and frees from strain. If there is a possibility of an intracranial expanding lesion being

present, remove only 1 c.cm. for estimation of cell, globulin and total protein contents; the other tests can wait. If the first few drops of fluid are blood-stained they should be discarded and a specimen collected as soon as the fluid runs clear. Except in cases of subarachnoid hæmorrhage, the blood in the fluid should never be greater than a few drops at the beginning of the flow. Any greater amount should be regarded as a sign that the operator's methods need revising. Almost the only contra-indication to lumbar puncture is skin sepsis in the lumbar region. Even in spinal epidural abscess lumbar puncture is permissible if insertion of the needle is stopped directly pus is encountered.

Ventricular puncture is sometimes indispensable, but it should be performed only by those who are thoroughly conversant with the minute anatomy of the parts. Cisternal puncture is fraught with danger from two sources—when the needle point lies in the cisterna magna the distance between it and the medulla oblongata is very small and the margin of safety exceedingly narrow; and abnormal blood vessels in the path of the needle just inside the foramen magnum are too common and too dangerous to be ignored. Reid urges that all necessary information can be gathered from lumbar and ventricular puncture, and that, in view of its dangers, there is no essential use for cisternal puncture. There was a time, in the treatment of purulent meningitis by serum, when it was legitimate in some cases to run the risks of cisternal puncture. That time has passed, and most will now agree that, apart from encephalography, the indications for cisternal puncture are scanty.

Oliguria in Blackwater Fever

By B. G. MAEGRAITH

and

G. M. FINDLAY

(Abstracted from the *Lancet*, ii, 23rd September, 1944, p. 403)

THE oliguria of blackwater fever may be in part due to peripheral vascular atonic collapse with subsequent redistribution of intrarenal blood flow and depression of glomerular filtration. Blockage of the renal tubules does not appear to be the deciding factor. The degenerative changes seen in the renal epithelium are probably assisted by anoxia resulting from inadequacy of the altered circulation.

The part played by hæmoglobin in the production of oliguria and anuria in blackwater fever is not established. The recorded effects of circulating hæmoglobin on the kidneys in animal experiments vary with the observer, but it has been shown that large amounts of hæmoglobin can pass through the kidney without inflicting serious damage on the organ. It appears likely, therefore, that the kidney lesions seen in blackwater fever, etc., are not primarily the result of damage due to the passage of hæmoglobin. The effects of the passage of similar amounts of hæmoglobin upon tissues already damaged by circulatory failure, or by some circulating chemical substance, have yet to be determined. The hæmoglobin may prove to have no other effect than that of pigmenting already existing casts and necrotic debris.

The cause of the vascular collapse which we believe occurs in blackwater fever is unknown. It may be the same factor as that which influences the balance between lytic agent and inhibitor, and so gives rise to the excessive red-cell lysis, or it may be something entirely different. In any case we consider that one of the fundamental features of blackwater fever is a lowering of the tone of the peripheral vascular system and that anuria is a manifestation of the ultimate vascular collapse.

Blockage of the renal tubules with debris and hæmoglobin products is not the deciding factor in the production of oliguria in blackwater fever.

Observation of the reactions of the skin to stroking, and of the hepatic vessels at autopsy, suggest that peripheral vascular atony is present in blackwater fever, and it is suggested that this plays a part in the production of oliguria by a redistribution of the renal blood flow.

The changes found in the renal epithelium are thought to be due to anoxia.

The Electron Microscope : Its Application to Medicine

By G. E. DONOVAN

(Abstracted from the *Proceedings of the Royal Society of Medicine*, Vol. XXXVII, October 1944, p. 708)

It is now possible to obtain electron micrographs of the location of certain chemical reactions incident to the metabolism of the bacterial cell. The reduction of potassium tellurite by *C. diphtheriae* has been studied. It has been demonstrated that tellurium crystals form in all parts of the micro-organism, in some cases puncturing its walls. A method of selective microchemical analysis has been developed by taking electron pictures of bacteria after exposure to salts of heavy metals. The electron microscope has demonstrated changes in the bacterial cell brought about by the action of germicides and antibacterial substances. The recording of the action of germicide agents on individual bacterial cells is a promising field of application of microchemical analysis.

Electron micrographs of bacteria have been published. The *Mycobacterium tuberculosis hominis* shows that its cell wall appears to be very delicate. Many small dark granules appear throughout the field and, in particular, adhering to the cell wall. Large black granules are shown within the protoplasm. A strain of *Fusobacterium* shows dense areas, but in contrast to that of the tubercular bacilli the dense areas are not localized in definite circumscribed granules. Monotrichates, for instance, *Vibrio schuylkilliensis*, show a cell wall. Definite circumscribed granules are again seen with the protoplasm. The flagella of monotrichates—for example, vibrios—are on the whole wider in diameter than those of peritrichate and lophotrichate species. Unstained diphtheria bacilli show definite polar bodies. *Treponema pallidum* appears to have flagellate processes at various points along its course. The morphology of *Leptospira ictero-haemorrhagiae* and *L. canicola* has been investigated.

If suspensions of streptococci are subjected for a short period of sonic vibrations some of the cells are cytolysed. These bacteria retain their original outline, but become transparent to the electron beam, appearing as pale grey bodies and contrasting strongly with the opaque normal cell. *B. subtilis*, after subjection to sonic vibrations, shows the flagella to be continuous with the cell wall.

The combination of antibodies with flagellar and somatic antigens has been demonstrated by the electron microscope. It has long been known that the bacterial cell wall and flagella of organisms such as the bacilli of typhoid and paratyphoid are altered by the deposition of antibodies, and the combination of antibodies and antigens at bacterial surfaces has also been shown by quantitative analytical methods. These sensitized surfaces have now been examined under the electron microscope, and, as a result of the deposition of homologous antibodies upon them, the walls are found to become opaque, and less clear-cut in outline. The flagella become thicker, but less sharp and less uniform in outline, and they tend to coalesce.

The various viruses differ greatly in size, although each kind of virus is itself very uniform in size. During the last decade, a few of the viruses which attack plants have been isolated. Although they differ from each other in stability and analytical composition, all those purified have been shown to consist solely of

nucleoproteins of high molecular weight. These viruses seem to be a connecting link between living and non-living matter. They are actually protein molecules possessed of certain definite biological activity. On the other hand, there are viruses, that of vaccinia, for example, and all the Rickettsia disease agents, which are very much larger, and cannot be regarded as single molecules. The larger viruses appear to be true micro-organisms which can only live a parasitic existence. One of the first viruses to be photographed under the electron microscope was that of tobacco mosaic, and it at once confirmed the suggestions, based on other methods, about the size and shape of this virus. It was a long rod about 300 mμ. Particles of tobacco mosaic virus appear in purified form as discrete rod-like units with a tendency to side-to-side and end-to-end aggregation. The electron microscope has also been used in the study of the virus of tomato bushy stunt. The reaction between tobacco mosaic virus and its antiserum has been studied by means of the electron microscope. This instrument has been used in the investigation of the morphological structure of the virus of vaccinia. The elementary bodies of vaccinia are rectangular shaped, resembling a brick, and contain five areas of condensation, and are somewhat like the five spots of a dice. Sharp and his colleagues have employed the electron microscope in their investigations of western strain equine encephalomyelitis virus. Taylor and his associates have used this instrument on the eastern strain equine encephalomyelitis virus. Studies have been published on the nature of the virus of influenza with particular reference to the dispersion of the virus of influenza A in tissue emulsions, and in extra-embryonic fluids of the chick. The size of the infectious unit in influenza A has been investigated. This instrument has been employed on the morphological structure of Rickettsia. It has also been used in studies on the papilloma virus protein.

Studies of bacteriophages disclose an extremely constant and characteristic sperm-like appearance with a round head, and a much thinner tail; in many micrographs the head is filled with a dense internal structure. These are absorbed to their specific micro-organisms by head or tail, and after contact it is possible to observe extensive damage of the bacterial cell. These results are interesting, as some years ago the bacteriophage was looked upon by some workers as of macromolecular nature. The discovery of such constant and detailed information is of interest also to geneticists, for genes are thought to be macromolecular entities. The sperms of the ram and bull, being extremely flat, lend themselves to examination and have already come under observation.

The electron microscope is of value in histological research. It has revealed characteristic cross-striations in collagen fibres and the effects of various physical and chemical conditions on the fibres have been investigated in a search for further knowledge of the molecular structure of collagen. To entomologists, this instrument shows hitherto unseen structures, and it allows the accurate measurement of those already recognized. The trachea, trachioles, air sacs, wing scales, and cuticle have been examined, and experiments on the mode of penetration of the cuticle by non-volatile oils serve as an example of future useful applications.

The foregoing are only some of the many fields in which an electron microscope is useful.

Massive Arsenotherapy for Syphilis

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXVI, 28th October, 1944, p. 554)

1. THE therapeutic results in a group of 4,351 massive arsenical treatments for syphilis have been studied.

2. It was found that the best results (excluding the highly reactive slow intravenous drip administration of

nearsphenamine) followed the use of multiple syringe injection of mapharsen combined with typhoid vaccine.

3. The most effective massive arsenotherapy yields 85 to 90 per cent of satisfactory results in primary syphilis and 70 per cent in secondary syphilis.

4. About 5 to 6 per cent of the primary cases relapsed and 10 to 13 per cent of the secondary cases.

5. Patients treated when the titre of the Kahn quantitative test on the blood was 20 units or below experienced more frequent satisfactory results and fewer clinical relapses than did cases with a titre than 20 units.

6. Results were slightly better among patients receiving larger doses of arsenicals than among those receiving smaller doses.

7. The administration of bismuth during the period of treatment appeared to improve the results obtained.

8. The following differences in response to treatment were noted: Patients over 25 years of age responded better than those under 25; males responded better than females; whites responded better than non-whites.

9. Least satisfactory results to treatment were obtained among young non-white females.

10. Acute encephalopathy was observed in 7.1 per thousand treatments. Of these 3.2 per thousand were fatal and 3.9 per thousand were followed by recovery. No difference could be demonstrated between treatments with regard to the frequency of this type of reaction.

The Use of Penicillin Pastilles in Oral Infections

By A. B. MACGREGOR

and

D. A. LONG

(Abstracted from the *British Medical Journal*, ii, 25th November, 1944, p. 686)

PENICILLIN included in a pastille under suitable conditions of manufacture is liberated in the mouth in an active form. The concentration in the mouth can be maintained and the pastille kept for a period of at least three months without appreciable deterioration or loss of efficiency of the penicillin. It is simple to use and is well tolerated even by children. (The youngest patient receiving pastilles was aged 5.)

Acute ulcerative gingivostomatitis (Vincent's type) can be treated more simply and more quickly with the use of penicillin pastilles than by any other method. In addition, the loss of tissue caused by the more usual treatments with caustics and escharotics can be avoided. It is not suggested that gingivectomy or other procedures to eliminate the gum pockets and stagnation areas will not be necessary at a later date, since, while these pockets and areas remain, the possibility of recurrent infection is always present. The treatment described is advocated in the acute stages, and the fact that no recurrences have been seen over a period of three and a half months suggests that immediate recurrence is unlikely. In view of the fact that intravenous arsenicals are still widely employed in the treatment of the disease in spite of much evidence to show that it is ineffective, we consider that it is worth drawing attention to the fact that three of our most severe cases have been undergoing treatment for syphilis with injections of bismuth and intravenous arsenicals.

Patients with acute hæmolytic streptococcal tonsillitis, including four with scarlet fever, seemed to respond clinically to treatment with pastilles. The effect on the throat flora appeared to be rapid, but, even so, a larger series of cases is necessary before any final conclusions can be drawn. The early disappearance or reduction in numbers of hæmolytic streptococci in the throat after treatment had started suggests that the risk of droplet infection is greatly reduced, and we regard this point as of importance epidemiologically.

The treatment of throat carriers of hæmolytic streptococci proved disappointing, as was anticipated. Nevertheless, it is of interest that they became negative while undergoing treatment, and in the case of the medical student described, this fact proved of practical value.

In the small series of patients so far treated it appeared that surgical conditions of the mouth and throat could be kept free from pathogenic organisms during administration of the pastilles, with marked symptomatic relief.

On bacteriological grounds faucial diphtheria should be an indication for treatment with penicillin pastilles. Unfortunately, we have as yet been unable to obtain suitable cases, but it is hoped to publish these results later in a fuller report.

New Drug Active in the Chemotherapy of Experimental Gas Gangrene

By D. G. EVANS

and

OTHERS

(Abstracted from the *Lancet*, ii, 21st October, p. 523)

Two new drugs, *p*-methylsulphonylbenzamidine hydrochloride (V187) and *p*-methylsulphonylbenzylamine hydrochloride (V335), have been synthesized and found to have a potent local chemotherapeutic action in experimental gas-gangrene infections in guinea-pigs. Their action is not inhibited by *p*-aminobenzoic acid.

An extended study of V187 has demonstrated its effectiveness against *Cl. welchii*, *oedematiens* and *septicum* infections. It is well tolerated when given intramuscularly in therapeutic doses. *In vitro* and in the mouse, V187 is as effective against sulphanilamide-resistant streptococci as it is against a sulphanilamide-sensitive strain.

In guinea-pigs, V187 is rapidly absorbed and excreted after intramuscular and intraperitoneal administration. Given orally, it is but poorly absorbed.

Death Due to Estivo-Autumnal Malaria A Resume of One Hundred Autopsy Cases 1925-1942

By B. H. KEAN

and

J. A. SMITH

(Abstracted from the *American Journal of Tropical Medicine*, Vol. XXIV, September 1944, p. 317)

1. THE record of 100 patients who died of estivo-autumnal malaria and upon whom autopsies were performed at the Board of Health Laboratory, Gorgas Hospital, Ancon, Canal Zone, between 1925 and 1942 were reviewed. One and six-tenths per cent of all autopsies (6,214) performed during that period were on patients who died of estivo-autumnal malaria.

2. Deaths occurred in all months, although questionable peaks in May-June and December-January were present.

3. Of 39 Panamanians in the series, 34 were children of 10 years or younger.

4. The duration of symptoms before hospitalization varied from four and one-half hours to twenty-one days. Twenty-three patients had symptoms of not more than one day before hospitalization and yet they died.

5. The degree of parasitization of the peripheral blood was not a wholly adequate index of the seriousness of the illness since 12 patients with light infections died within twenty-four hours of admission despite heavy treatment with quinine.

6. Some of the classical signs and symptoms of malaria such as chills, headache, vomiting, palpable liver, and spleen were absent in one-third to one-half of the patients.

7. The clinical and pathological changes which have been described in shock were recorded in one-third of the patients upon whom classification of the type of death was possible.

8. No correlation between cerebral malaria as noted clinically and cerebral plugging as recorded at autopsy was apparent in our material.

9. Two case reports illustrating the occurrence of shock in patients with malaria were presented. Anti-shock measures were believed to have saved the life of one patient.

The Biosynthesis of Riboflavin in Man

By V. A. NAJJAR

and

OTHERS

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXVI, 7th October, 1944, p. 357)

1. TWELVE experimental subjects, placed on an experimental diet of purified vitamin-free foods, in which only supplements of pure vitamins were given, subsisted for a period of twelve weeks on a diet containing between 60 and 90 micrograms of riboflavin per day.

2. The excretion of riboflavin in the urine, after a preliminary drop, tended to remain constant at a value roughly twice that of riboflavin intake. The faecal excretion remained unaffected at a level of five to six times the intake, a phenomenon which can be attributed to synthesis or by the intestinal bacteria.

3. An attempt to inhibit the biosynthesis of riboflavin by the intestinal bacteria by the administration of succinylsulfathiazole for a period of four weeks met with no success.

4. The conclusion is drawn that riboflavin may not be a dietary essential under all conditions. The conditions in which it may be effectively synthesized in the intestine remain to be defined.

Reviews

ROSE AND CARLESS' MANUAL OF SURGERY.—By Cecil P. G. Wakeley, C.B., D.Sc., F.R.C.S., F.R.S.E., F.R.S.A., F.A.C.S., F.R.A.C.S., and John B. Hunter, M.C., M.Ch., F.R.C.S. Seventeenth edition in two volumes. Volume XX and 840, Volume II, 926. With 30 plates and 1,100 illustrations. Baillière, Tindall and Cox, London. Price, 35s.

THIS book is a very old and dear friend to many members of the profession. Originally published nearly 50 years ago it has been revised and rewritten several times and is now in its 17th edition. It has maintained its place as possibly the best book of its kind for students and practitioners. The title of the book, however, raises the question: when does a manual cease to be a manual—or a handbook? We do not see how any work of 1768 pages in two volumes can be called a manual.

Most of the book in its present form is the work of C. P. G. Wakeley and J. B. Hunter but of the fifty-one chapters eight are written by others, five by V. E. Negus and one each by Vernon Hall, E. Holland, Bishop Harman and Sir Frank Connor.

The preface to the 17th edition states: 'The book has been revised but not as thoroughly as we should

have liked', war time activities and conditions having made a more thorough revision difficult. In spite of the difficulties, it does seem a pity that a book published in 1944 should contain only nine brief references to the use of sulphonamides and no reference whatever to their use in abdominal surgery. More might have also been made of the use of blood transfusion in surgery. Other matters which have recently come to the fore are hardly dealt with adequately. The difficulty is in these days not only that of authors and writers being engaged in war activities, and that of difficulties in paper and printing, but also that caused by the fact that knowledge is growing so rapidly that in certain respects many books are out of date before they are published.

It is expected that the next edition of this book will be much more thoroughly revised and brought up to date.

The book is most excellently produced for a war time publication, and it contains 1,100 illustrations, most of them are excellent.

PYE'S SURGICAL HANDICRAFT.—Edited by Hamilton Bailey, F.R.C.S. (Eng.). Pp. 628 plus xl. Fourteenth Edition. 1944. John Wright and Sons Ltd., Bristol. Price, 25s.

THIS book first published 60 years ago, now in its fourteenth edition, is better than ever. The principal changes between this and the previous edition of 1942 are the inclusion of a large number of new illustrations of technical procedures, and these illustrations have enabled the editor to devote less space to the description of the procedure illustrated. Detailed review is impossible and unnecessary. The 604 pages of this book contain a mass of information clearly and interestingly presented and well illustrated. The book is essential to medical students and to budding surgeons, and even experienced surgeons will find much of value in it.

THE SURGERY OF ABDOMINAL TRAUMA.—By Geoffrey E. Parker. Pp. 120. J. and A. Churchill, Ltd., London. Price, 10s. 6d.

THIS little book is based mainly on a personal study by the author of 94 cases of abdominal wounds in the Mediterranean zone. It includes a chapter on diagnosis, one on pre-operative treatment and resuscitation, one on general operative considerations and a longer chapter on technique of the repair of the abdominal viscera; a short chapter of 7 pages on statistics and 53 pages of case notes. The booklet is full of touches based on recent practical experience and the discussion of the cases is refreshingly frank; failures and mistakes are fully admitted.

HANDBOOK OF DIAGNOSIS AND TREATMENT OF VENEREAL DISEASES.—By A. E. W. McLachlan, M.B., Ch.B. (Edin.), D.P.H., F.R.S. (Edin.). Pp. 364 plus viii. E. and S. Livingstone, Edinburgh. Price, 15s.

In the preface, the war time increase in venereal disease is discussed and the importance of sound clinical instruction of under-graduate and post-graduate students for whom this book is intended is stressed. The book fills this purpose admirably. It contains 159 illustrations some of them being in colour. The use of the sulphonamides in treatment is fairly fully discussed but penicillin does not seem to be mentioned. An admirable booklet but with the present rapid developments, one that may quickly need revision.

THE MODERN TREATMENT OF SYPHILIS.—By Joseph Earle Moore, M.D. Pp. xli and 717. Second Edition. Third printing, 1944. Baillière, Tindall and Cox, London. Price, 38s. 6d.

THIS book published in 1933 is now in the third printing of its second edition. In the last printing in



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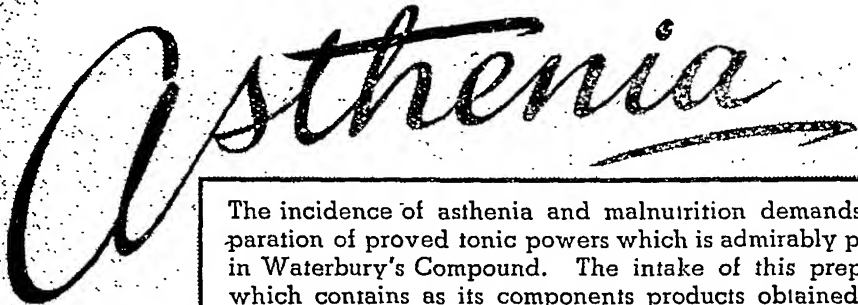
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May 1943 two new chapters appeared; one on intensive arsenotherapy of early syphilis and another on venereal disease control in the army. This large book of 625 pages is obviously not intended for the student or the ordinary practitioner but for specialists on the subject, or as a book of reference. It is an exhaustive discussion on the subject and each chapter is followed by an extensive bibliography. As with other books on this subject one surmises that new revised editions may soon be needed.

VARICOSE VEINS, HÆMORRHOIDS AND OTHER CONDITIONS: THEIR TREATMENT BY INJECTION.—By R. Rowden Foote, M.R.C.S., L.R.C.P., D.R.C.O.G. Pp. viii and 128. H. K. Lewis and Co., Ltd., London. Price, 12s. 6d.

THIS excellently written and produced booklet of 115 pages by the physician in charge of the Injection Clinic of the Royal Waterloo Hospital gives a very good account of this form of treatment, its applicability and its limitations. The book however deals not only with injection treatment but with operative treatment of varicose veins; the chapter on operative treatment has been written by Rodney Maingot; this chapter condemns the procedure of percutaneous and subcutaneous ligation which was first used in the eighteenth century and which various recent workers have attempted to revive. High open ligation with subsequent injection, the patient being ambulatory six hours after an operation, is strongly advocated. There is also a chapter on varicose ulcers and an appendix on elastoplast bandages. An excellent little book.

AIDS TO CLINICAL PATHOLOGY.—By David Haler, M.B., B.Sc. (Hons.). Pp. viii and 358, 21 illustrations. Baillière, Tindall and Cox, London. Price, 6s.

THE scope of this book is best explained in the preface:

'This small textbook is intended to be used by students and others interested in laboratory work. It attempts to give techniques which have been found to work in actual laboratory practice. As far as possible alternative methods are described for most estimations. No attempt has been made to cover some of the more refined hematological procedures, neither has any detailed attention been paid to the care of animals nor to streptococcal grouping.

The book as it stands is a combination of the old "Aids to Pathological Technique" with the "Aids to Practical Pathology" and I have tried to maintain the good points of both volumes.'

The author appears to have adequately attained these objects and has produced a most useful little book of such a size that it can be easily slipped into the pocket.

HALE WHITE'S MATERIA MEDICA, PHARMACY, PHARMACOLOGY AND THERAPEUTICS.—Revised by A. H. Douthwaite, M.D., F.R.C.P. Twenty-sixth Edition. 1944. Pp. 594 plus ix. J. and A. Churchill Ltd., London. Price, 14s.

THIS book, now in its 26th edition, has been thoroughly revised, and it now contains information on the sulphonamides, anticoagulants, hormones, and penicillin. It also contains references to the important drugs described in the 5th and 6th addenda to the British Pharmacopœia. On the whole, a most excellent book but some of the sections on the therapeutics of tropical diseases need revision by writers with first-hand knowledge of the subject.

A MANUAL OF DISEASES OF THE EYE.—By Charles H. May, M.D., and the late Claud Worth. Ninth Edition revised by M. L. Hine, M.D. (Lond.), F.R.C.S. (Eng.). 1944. Baillière, Tindall and Cox, London. Pp. viii plus 538. Illustrated. Price, 16s.

THIS book was first published nearly forty years ago, and maintains its deserved popularity as a standard

textbook of moderate length for students and general practitioners. In spite of the war, it is still well printed on good paper and is easy to read. It is profusely illustrated with 371 photographs, drawings and coloured plates.

One excellent feature of the book is the arrangement of the anatomical and physiological descriptions. The anatomy and physiology are placed at the commencement of each chapter instead of being done *in toto* at the beginning of the book.

There is a chapter on tropical ophthalmology which will be useful to students in India. Mention of 'epidemic dropsy glaucoma' and 'epidemic superficial punctate keratitis' might be included in this chapter. In the chapter on glaucoma the term 'congestive or inflammatory' is used. It would seem that the word 'inflammatory' should be dropped as it is confusing to the student when trying to understand the difference between acute congestive glaucoma and iritis with secondary tension. In the chapter on ocular therapeutics it would be easier to remember doses if all examples of drops and ointments were given as made up to one ounce instead of showing them up in varying quantities.

The present edition has been brought up to date by additions on the use of the sulphonamides and penicillin in ophthalmology, vitamin B₂ and the modern view of malignant melanoma of the choroid.

The book can be thoroughly recommended.

E. J. S.

REVELATION OF CHILDBIRTH: THE PRINCIPLES AND PRACTICE OF NATURAL CHILDBIRTH.—By G. D. Read, M.A., M.D. (Camb.). 1943. Second Edition. William Heinemann Medical Books Limited, London. Pp. x plus 246. Illustrated with 6 plates. Price, 21s.

'REVELATION of Childbirth' by Dr. Dick Read is described on the cover as a book for every expectant and prospective mother but it should be read by all members of the medical and nursing professions who undertake midwifery practice. Several chapters in the book have in fact been written primarily for medical men and women.

Dr. Read's premises is that pain is not a normal accompaniment of a physiological process and that pain therefore seems out of keeping with the laws of Nature in a process so vital to the survival of the race as reproduction.

Dr. Read's early scientific training gave him an interest in 'the influence of the sympathetic nervous system upon the activities of the viscera, the interpretation of painful stimuli, the visceral reactions to emotional states', which he has used to good purpose in interpreting the problem of pain during confinement in indicating how pain can be eliminated.

The book is stimulating not only because of the success which has attended the methods advocated, but because of the evidence it affords of questioning much of the accepted teaching of past generations, the deductions made from acute and careful observation of the phenomena of labour, and the indication of new fields for exploration and investigation in the achievement of painless childbirth and radiant motherhood.

J. M. O.

THE NATURAL DEVELOPMENT OF THE CHILD. A GUIDE FOR PARENTS, TEACHERS, STUDENTS AND OTHERS.—By Agatha H. Bowley, Ph.D. Second Edition. 1943. E. and S. Livingstone, Edinburgh. Pp. xvi plus 184, with 84 photographs. Price, 8s. 6d. Postage, 6d.

'THE Natural Development of the Child' is written from the psychologist's point of view. It deals mainly with the development of the character and personality of the child though the close linkage of physical and intellectual development naturally necessitate attention

being given also to these aspects particularly in infancy and the pre-school years.

Very few books written for the layman trace the social and emotional development of the child from birth to adolescence and the bird's eye view which the book gives is valuable. The ground covered is wide and the treatment therefore thinly spread but there are good lists for further reading at the end of each chapter.

A number of technical terms are used throughout the book which may cause difficulty if the glossary placed at the end is not noticed early by the reader.

The book aims to increase the general psychological knowledge of parents and teachers and to help them better to understand the children under their care; it admirably achieves its purpose, and can be safely recommended, as sound introduction to the fascinating study of the child's social development, and to the management of the difficult child.

A chapter on children and the war has been added to this second edition of the book first published in 1942.

J. M. O.

STRUCTURE AND FUNCTION AS SEEN IN THE FOOT.—By Frederic Wood Jones, D.Sc., F.R.S., F.R.C.S. Pp. iv and 330, 150 illustrations. Baillière, Tindall and Cox, London. Price, 25s.

PROFESSOR Jones recently published a book on the 'Principles of anatomy as seen in the hand'. This volume on the foot is in some way a supplement to the one on the hand. These books and the other writings of this author are characterized by a desire to get away from the anatomy of the dead to the structure and function of the living, by an original and interesting approach to the subject, and by lively and interesting presentation. These points are well illustrated in the book under review.

After a lively but brief introduction followed by a discussion of the principles of anatomical terminology in which the author expresses the view that much present terminology is quite irrational, there follow chapters on the foot in phylogeny, in ontogeny, chapters on digital formulæ and metatarsal formulæ. These formulæ relate to relative sizes of the digits and the metatarsal bones; then follow chapters on external characters including flexure lines, cleavage lines, papillary ridges, and hair. In the subsequent chapters are discussed the fasciæ and bones, accessory bones, sesamoid bones, joints, extrinsic and intrinsic muscles and their action, tendons, tendon sheaths and bursæ, the arches of the foot, the innervation of the foot and the vascular channels. The book is illustrated by 150 line drawings. Each chapter is followed by a brief list of suggested references for further reading. Any detailed review of this book is out of the question. The author has succeeded in giving a most interesting and stimulating account of structure and function as seen in the foot. This is a book which can be strongly recommended to students of anatomy and to surgeons.

J. L.

Abstracts from Reports

REPORT OF THE EUROPEAN MENTAL HOSPITAL AT RANCHI, FOR THE PERIOD, 1ST APRIL, 1943, TO 31ST MARCH, 1944

DURING the year the number admitted was 121 (91 males and 30 females), which with the previous year's 'remaining' totalled 390. Of the new admissions, 94 were between 20 and 40 years, and 20 between

40 and 60 years of age. About 30 per cent of the patients had schizophrenia including dementia præcox, next in order came those with paranoid states, mental deficiency, neurosis and psychoneurosis, maniac depression, etc. The predisposing causes were stress of military service, worries, heredity, etc., but in a good many cases the causes could not be ascertained. During the year, electric shock therapy was employed and most encouraging results were obtained in psychoneurotics. 'The method is technically effective, simple and no fear or hostility in the patients.' Formerly chemical methods were employed, but the chief drawback was a feeling of horror and apprehension by the patient during the few seconds between the injection and unconsciousness.

THE PASTEUR INSTITUTE OF SOUTH INDIA, COONOR. ANNUAL REPORT, 1943-44

ANTI-RABIC treatment was given to 13,280 patients at the institute and the subsidiary treatment centres, and in addition, routine laboratory examinations were carried out on a large scale. The study of the parasite, originally found in the mid-brains of guinea-pigs experimentally infected with rabies street virus, was continued; it appears to be a protozoon and may be connected with the ætiology of rabies. The Negri bodies may represent a stage in the life-cycle of the parasite. An investigation is in progress on tropical eosinophilia; the findings so far do not support the existing theories about its ætiology, i.e. environmental, allergic or leukæmia, but support the possibility of an infection being responsible for the syndrome.

Work carried out by the Nutritional Research Laboratories included (1) analysis of foods, chiefly with reference to vitamins, (2) animal experiments: massive doses of vitamin C had no effect on fluorine poisoning in rats, thus failing to support the conclusions of Pandit and his colleagues that lack of this vitamin is a contributory factor in the causation of chronic fluorosis in man. Experiment was made to find out whether rats which do not normally require vitamin C synthesize it in their intestine. Sulfasuxidine which destroys intestinal flora was given to rats fed on a diet complete except for vitamin C, but no evidence of its deficiency was found in the animals. (3) Clinical investigations. A type of nutritional diarrhoea marked by glossitis and histamine-fast achlorhydria responded well to the injections of nicotinic acid. Study of the relationship between dental caries and fluorosis, and investigations on infantile beri-beri are proceeding.

Correspondence

COMPLEMENT FIXATION TEST FOR KALA-AZAR

SIR,—I am glad to see, in October 1944 issue of the *I.M.G.*, that Dr. P. C. Sen Gupta, by reporting the results of a very large number of complement fixation tests, carried out according to the technique originally described by Greval, Sen Gupta and Napier (*Indian J. Med. Res.*, 27, 181), confirms the findings of those workers that the reaction is more specific for kala-azar than any other disease. The establishment of the value of the test in the diagnosis of early cases, when all other laboratory tests, except sternal puncture, are still negative is particularly significant. Dr. J. Lowe, in the same issue, rightly stresses the value of the test in the early diagnosis of kala-azar. The value of the

test has now been established beyond doubt and must take precedence over all other laboratory tests.

You, Sir, in your leader say that 'so far no person's name has yet been attached to this test, and it would appear better not to attach a person's name'. I do not agree with you. The value of the test is now fully established and it would be graceful to give credit to the original workers who described the technique and indicated its value in the diagnosis of kala-azar. The matter of precedence in this case is easily established. The first paper to be published which described a technique and definitely showed that the test was more specific for kala-azar than for leprosy or any other disease, was by S. D. S. Greval, P. C. Sen Gupta and L. E. Napier—*Indian J. Med. Res.*, 27, 181 (received for publication on 17th February, 1939). Before this two papers had appeared, first by S. D. S. Greval, J. Lowe and R. Bose, *Indian J. Med. Res.*, 26, 843 (received for publication on 8th September, 1938), the second by J. Lowe and S. D. S. Greval in the same issue of *Indian J. Med. Res.*, but received for publication on 12th September, 1938. But both these papers were concerned with the use of the complement fixation test in the diagnosis of leprosy and both sets of authors merely observed kala-azar as an interfering disease making the test non-specific for leprosy. Thus it was only after Greval, Sen Gupta and Napier published the paper referred to above that the value of the test in kala-azar was brought out in a definite manner, and a suitable technique for this test was described.

Therefore, Sir, in the best traditions of science the test should be named as Greval, Sen Gupta and Napier test.

Your obedient servant,
S. S. SOKHEY,
LIEUTENANT-COLONEL, I.M.S.

HAFFKINE INSTITUTE,
BOMBAY,
15th January, 1945.

[Editorial note.—It is good to have Colonel Sokhey's generous acknowledgment of the value of this work done in the School of Tropical Medicine, Calcutta; as one of the workers involved, the editor comments on this letter with diffidence, but the letter does appear in some ways misleading.

The editorial note quoted by Colonel Sokhey was written partly because it had been suggested that the editor's name should be attached to the test. To this the editor objected on the grounds stated below, although he personally did initiate this work on com-

plement fixation in Indian kala-azar with W.K.K. antigen.

The basis of the test was and is the work reported by Greval, Lowe and Bose, and by Lowe and Greval mentioned by Colonel Sokhey. This work, which was planned to include a check of Bier's report of positive findings in kala-azar, was initiated in the Leprosy Department and carried out in collaboration with Colonel Greval. The work clearly indicated that with W.K.K. antigen, complement fixation by the technique described was seen more constantly and in higher titre in kala-azar than in any other disease tested; also that positive results were seen early in the disease while in leprosy this was not so. Moreover, these findings in kala-azar were not incidental as Colonel Sokhey's letter would imply. The work was planned to cover kala-azar.

The later paper of Greval, Sen Gupta and Napier reported modifications of technique designed to increase specificity by diluting the serum, and later papers still, notably those of Sen Gupta, established firmly its diagnostic value. Actually, in most recent tests, the technique described by Greval, Sen Gupta and Napier has been used, but the antigen has been prepared by the W.K.K. method in the Leprosy Department of the School from the Stefansky bacillus and not the tubercle bacillus, as reported by Dharmendra and Bose of that department. Moreover, recently experiments have been made with a modified technique and a paper on this subject by Sen Gupta will shortly appear in our pages.

Thus the test is the outcome of the original work of Bier in South America, and of the later work of several workers in three different departments of the School.

Rather curiously, Napier was always critical of the work and even in his latest writing on kala-azar does not even mention it.

Of the three persons whose names Colonel Sokhey proposes to attach to the test, only one (Colonel Greval) had anything to do with the earliest phases of the work and with the first publications on technique and results. It is, however, correct to attach these three names to their particular technique they described later. We still have the Widal, Weil-Felix and Wassermann tests, although the technique of these workers is no longer used; we have the Kolmer technique and so on.

The editor still thinks that to attach the name of any one person or one group of persons to the basic test would be misleading. It is however correct to apply the three names mentioned to the particular technique described in their paper. The technique however may and almost certainly will change but we need not rename the test every time this happens.—
EDITOR, I.M.G.J

Service Notes

APPOINTMENTS AND TRANSFERS

MAJOR-GENERAL J. B. HANCE, C.I.E., O.B.E., is granted the local rank of Lieutenant-General, without effect on pay and pension. Dated 4th October, 1943.

The Viceroy and Governor-General has been pleased to make the following appointment on His Excellency's personal staff :—

To be Honorary Surgeon

Colonel (Tempy. Brigadier) D. V. O'Malley, O.B.E., 17th July, 1944, vice Colonel J. W. Vanreenen, O.B.E., vacated.

Lieutenant-Colonel K. S. Fitch, O.B.E., is appointed Assistant Director-General, Indian Medical Service (Personnel), with effect from the 8th January, 1945.

Lieutenant-Colonel J. H. Gorman, I.A.M.C., has been relieved of his duties as Director of Inspection in the Department of Food, Division III, with effect from the afternoon of the 15th February, 1945, for employment as Director of Public Health, Madras.

Major C. V. Ramchandani, I.A.M.C., Assistant Inspector of Hygiene in the Directorate of Inspection, Department of Food, Division III, has been appointed to officiate as Director of Inspection, with effect from the afternoon of the 15th February, 1945.

Captain M. D. Black, assumed charge as Professor of Midwifery in the King Edward Medical College, Lahore, and Medical Superintendent, Lady Willingdon Hospital, Lahore, on the forenoon of the 2nd February, 1945, vice Lieutenant-Colonel S. N. Hayes.

The undermentioned officers (on probation) are confirmed in the Indian Medical Service, with effect from the dates specified :—

Indian Medical Service (Permanent Commission)

Captain B. H. Sayed. Dated 17th June, 1940.
 Captain J. R. Vaid. Dated 24th June, 1940.
 Captain B. S. Khurana. Dated 1st July, 1940.
 Captain T. D. Chabiani. Dated 30th September, 1940.
 Captain R. L. Soots. Dated 10th October, 1940.
 Captain M. Shankhla. Dated 11th October, 1940.
 Captain T. J. Powell. Dated 5th December, 1940.
 Captain K. S. R. Menon. Dated 13th December, 1940.
 Captain I. Singh. Dated 27th December, 1940.
 Captain E. J. Crowe. Dated 23rd April, 1941.

*INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
 SECONDED TO THE INDIAN ARMY MEDICAL CORPS*

(Emergency Commissions)

To be Captains

19th December, 1944
 Rensto Gracias. Bhopindar Singh.
 20th December, 1944
 Eralil Mathai George. Ratneshwar Prasad Sinha.
 Madathil Munnathadathil Madhavan. Dated 21st December, 1944.

To be Lieutenants

Anil Baran Shome. Dated 18th October, 1944.
 Akul Jayachandran. Dated 19th November, 1944.
 Mohd. Hasan Arbab. Dated 1st December, 1944.
 Satyabrata Kundu. Dated 3rd December, 1944.

14th December, 1944

Nand Kumar Mehra. Gurdial Singh.
 Gul Hasan Pirzada. Dated 15th December, 1944.
 Shiv Kumar Gupta. Dated 17th December, 1944.

20th December, 1944

Kashi Prasad. Dhunjishaw Maneckshaw Marker.

The undermentioned officer of the I.M.S. (E.C.) reverts from I.A.M.C. and is seconded for service in the Royal Indian Naval Volunteer Reserve :—

Lieutenant S. G. Ramsaiya. Dated 27th December, 1944.

INDIAN MEDICAL SERVICE

*SECONDED TO THE INDIAN ARMY MEDICAL CORPS
 (Emergency Commissions)*

WOMEN'S BRANCH

To be Captain

Leela Thorat. Dated 15th December, 1944, with seniority from 20th May, 1940.

PROMOTIONS

Major to be Lieutenant-Colonel

E. G. Montgomery. Dated 22nd January, 1945.

Captains to be Majors

S. W. Allinson. Dated 13th January, 1945.

27th December, 1944

W. M. Niblock. P. A. Hubbard.
 T. P. Mulcahy. F. E. McLaughlin.

*SECONDED TO THE INDIAN ARMY MEDICAL CORPS
 Captain to be Major*

V. P. Patel. Dated 1st September, 1944.

*INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
 (Emergency Commissions)*

Lieutenant to be Captain

D. S. Krishnamurti. Dated 21st November, 1941.

RETIREMENTS

Lieutenant-Colonel I. B. Vaidya. Dated 31st December, 1943.

Lieutenant-Colonel A. H. Shaikh, C.I.E. Dated 5th February, 1945.

RESIGNATIONS

*INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
 SECONDED TO THE INDIAN ARMY MEDICAL CORPS
 (Emergency Commissions)*

Captain S. P. Das Gupta. Dated 20th October, 1944.
 G. Henderson, dated 11th January, 1945, and is granted the honorary rank of Captain.

RELINQUISHMENTS

*INDIAN MEDICAL SERVICE
 (Emergency Commissions)*

Captain B. Fife relinquishes her commission on account of ill health, dated 1st May, 1944, and is granted the honorary rank of Captain.

Captain E. R. James relinquishes his commission on account of ill health, dated 7th May, 1944, and is granted the honorary rank of Captain.

Captain J. S. Laurie relinquishes his commission. Dated 30th May, 1944.

*INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
 SECONDED TO THE INDIAN ARMY MEDICAL CORPS
 (Emergency Commission)*

Captain Sri Krishna Sen, dated 15th February, 1945, on grounds of ill health and is granted the honorary rank of Captain.

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Original Articles

M 3349 (PALUDRINE) IN THE TREATMENT OF HUMAN MALARIA

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and

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Introduction

M 3349 (or Paludrine) is an antimalarial compound prepared by Imperial Chemical Industries at their laboratories in Manchester. This firm's research workers tested it in birds, and it was considered that in bird malaria it was at least as effective as mepacrine. Studies of the action of this drug were undertaken under the auspices of the Medical Research Council in England by various workers in relapsing vivax malaria and in some cases of fresh falciparum infection in sailors. Results comparable with those obtained with quinine or mepacrine were reported, but some evidence of toxicity of the drug was encountered. One great difficulty of this work in England was that it was difficult or impossible to follow up the cases for sufficiently long to assess the relapse rate.

Major-General Bradfield, I.M.S., of the India Office arranged for consignments of the drug to be sent to India for trial and Major-General G. Covell, I.M.S., of the Malaria Institute of India, after testing the drug and finding it effective in monkey malaria, made the drug available for trial in the Calcutta School of Tropical Medicine. The main points which needed to be studied were (1) the toxicity of the drug, and (2) relapse rate after treatment with the drug.

Nature of the drug.—Details regarding the chemical composition of the drug are not available. General Covell states in a letter that in chemical composition this synthetic drug bears no resemblance either to quinine or to the sulphonamides. Also it is said to be much more easily produced than mepacrine. It is put up in tablets containing 0.2 gm. each. The tablets are white, easily soluble, and bitter in taste.

Dosage.—The work in England indicated that in the control of attacks of malaria a dosage of 3 tablets a day (0.6 gm.) for 7 days was

effective; half this amount (0.3 gm.) was not sufficient. With a dose of 0.6 gm. per day, toxic effects were few. In some cases in England, doses up to 1 gm. a day had been given, but toxic effects were reported as common. In view of these facts, it was decided to adopt a dosage of 0.6 gm. per day for adults in the cases treated here, but, as described later, our experience suggested that this dosage was possibly too big for the average Indian.

The patients treated.—Since one of the main objects was to study the relapse rate, which could only be done by keeping the patients under observation for several weeks after the treatment, and since most general hospital patients are unwilling to remain in hospital or under observation for this period, it was decided to try the drug in the treatment of malaria in the sick destitutes in Calcutta. Arrangements were therefore made to admit from the Narkeldanga Relief Camp for Sick Destitutes suitable patients suffering from malaria to the Carmichael Hospital for Tropical Diseases. Since they were homeless and destitute, the patients were willing to remain in hospital as long as was necessary.

It became obvious however that the number of patients that could be dealt with by this method was much limited by the length of their stay in hospital, with limited accommodation available, and therefore at a later stage arrangements were made for the treatment and observation of patients in the camp itself. Altogether up to the present time, 31 patients have been treated in the Carmichael Hospital for Tropical Diseases and 75 patients in the Camp for Sick Destitutes, Narkeldanga, Calcutta.

Many of the patients being 'sick destitutes', were in bad physical condition. Of the 31 patients treated in the Carmichael Hospital, only 6 weighed over 100 pounds. This fact may possibly have had an influence on some of the findings.

Methods of work in hospital cases.—Patients were selected who had marked rise of temperature and whose peripheral blood films showed a considerable number of malaria parasites. Even then, patients were not treated immediately but, if admitted to hospital, were, if possible, kept for a day or two without any treatment to make sure that the infection was a really active one, and not naturally subsiding.

Observation of the infection in hospital for a day or two before treatment, while possible in patients with vivax infection, was frequently impossible in those with a heavy falciparum infection for it would have endangered the patients' lives.

An attempt was made to get cases of fresh patients with a history of malaria of recent origin, if possible within the previous few days, and previously untreated. Patients with a long history of malaria and enlargement of the spleen were avoided.

Before treatment was instituted, during treatment, and after treatment, four-hourly temperature records were kept, and daily blood films were made and examined; and, in many cases during the fever, twice daily blood films. It was thus possible to study accurately the time taken to control the fever, and the time taken for the parasites to disappear from the peripheral blood. Moreover, the patients were kept under observation for periods of five weeks or more, with 3 exceptions in the 31 cases treated in the hospital. It was thus possible to detect the early relapses although some later relapses may have been missed. No other treatment was given except M 3349.

Discussion of results in hospital cases

(1) *Toxicity of the drug.*—In several cases treated in the Carmichael Hospital, the occurrence of nausea and vomiting immediately following the administration of the drug was recorded. It is difficult to say to what extent the malaria itself contributed to the causation of the symptoms, but of course malaria does frequently cause such symptoms. These symptoms were however experienced mainly early in the experiment when the dosage of one tablet three times a day was being used for an adult. Later in the experiment, when the dosage was reduced to two tablets a day, such symptoms became less common. These symptoms alone however were not the main cause for concern. Two deaths were recorded of patients under treatment with this drug. The notes of these two cases are given below.

Case 1.—Sasi Bagh, an old man aged 60, general condition poor; history of malarial fever two months ago and of dysentery with blood and mucus in the stool six weeks ago. For the last seven days he had fever with chill and rigor daily and severe headache. On admission, temperature 102°F., pulse 120; respiration 26; scattered râles were found throughout the lung. The spleen was palpable.

The blood showed numerous M. T. rings and crescents. Treatment with M 3349 was instituted at once and symptomatic treatment was given for his cough. On the second day, his temperature rose to 104°F., and respiration rate to 32. The fever persisted next day but was not intermittent and the blood showed scanty M. T. rings and quartan parasites. On the third day the fever became continuous, but the blood showed no asexual forms of malaria parasites. His condition was bad, the pulse rate rising to 120 and the respiration rate to 40. The systolic blood pressure was 75 and the diastolic 40. The administration of M 3349 was stopped and sulphapyridine was given for the next five days. During this time he vomited altered blood in small amounts and this continued till the end. Shortly after the administration of sulphapyridine, the temperature fell to normal and the general condition improved and for the next seven days he was afebrile but was drowsy and incontinent of urine. The blood urea and non-protein nitrogen were raised. The urine showed traces of albumen but no casts; some pus cells were present. Blood pressure rose to 102/60. For the next five days he showed evening rises of temperature and his condition remained poor. He died 16 days after admission to hospital and 13 days after the cessation of M 3349. The only significant finding seen at post-mortem was sub-mucous hæmorrhage of the whole of the small intestine, and fatty liver and fatty heart.

Case 2.—An old man aged 65, general condition poor, but blood pressure 125/85. He had a history of fever with chill and rigor, headache and vomiting for three days. Liver and spleen were not palpable. He showed a heavy infection with *P. vivax*. On the evening of the day of admission, the temperature was 104°F., falling to normal the next morning. Treatment was instituted on the next day; he had another rise of temperature to 104°F., falling to normal next morning. On the second day of treatment, his temperature again rose to 103.5°F. but ceased to be intermittent and by this time the blood showed few parasites. He became incontinent of urine and fæces and also developed diarrhoea. On the third day of treatment, the blood showed few parasites but he had remittent temperature 103.5 to 100°F. On the fifth day in hospital and the fourth day of treatment his condition deteriorated, the blood pressure fell to 80/55 and in the evening he died. For the last two days he showed no asexual form of the parasite in the blood. Post-mortem examination showed pneumonia at the base of the right lung and sub-mucous hæmorrhage in the gall bladder; neither of these findings appeared to be sufficient to cause death.

Both these patients were old men weighing 86 and 85 pounds, admitted from the Camp for Sick Destitutes. Their physical condition was far from good. Both of them had lung complications but in neither did these seem sufficient to cause death, and it appears possible that the drug contributed to the death in both these cases. It is true that in the first case death did not occur for 13 days after the

discontinuance of the drug, but the cause of the death appeared to be the condition of the small bowel which became apparent shortly after the drug was discontinued.

Because of these fatalities, the dosage of the drug in the further cases treated was placed on a lower level, and care was taken in hospital not to treat patients in very bad physical condition. No further trouble was experienced in the hospital cases, and moreover the lower dosage did not seem to reduce the efficacy of the treatment.

(2) *The effectiveness of the drug in controlling the attack.*—In practically all the cases, the fever was promptly controlled and the asexual forms disappeared promptly from the peripheral blood. The results however varied a little according to the species of plasmodium.

(a) *Vivax infection.*—Of the 31 cases treated in the hospital 19 showed infection with *P. vivax*. In all cases except one, the temperature was normal in 48 hours, and the asexual parasites disappeared from the peripheral blood usually within a further 24 hours. In some cases however, gametocytes persisted, usually for a day or two, but in two cases for 6 days. During this time however the patient was quite afebrile and no asexual forms were present. The effect of the drug in controlling *P. vivax* infection thus appears to be good, comparable to that obtained by comparable doses of quinine and atabrin; as with quinine and atabrin, the effect is much more marked on the asexual forms.

(b) *Falciparum infection.*—Of 31 patients treated in the hospital, 17 showed *P. falciparum* infection. In this infection in all cases except one the temperature was normal within 48 hours, and in a further 24 hours the peripheral blood showed no asexual parasites. In only one or two cases were asexual parasites found for more than three days. The action of the drug in the control of malaria due to *P. falciparum* was even more marked than in *P. vivax* infection. Clinically and parasitologically the results of the treatment appeared excellent.

(c) *Quartan infection.*—Only 3 cases of the 31 cases treated in the hospital showed infection with *P. malariae*. One of these patients died as described above. In one the fever became less but did not entirely disappear and the parasites persisted during the whole course of treatment; but in the third case asexual

forms of the quartan parasite disappeared in 56 hours, although the temperature was normal in 48 hours; the gametocytes however persisted for two weeks.

Thus the results of treatment in quartan malaria appear to be variable. The same is true of treatment with quinine and atabrin.

(d) *Mixed infections.*—Of the 31 patients in the hospital, 8 showed mixed infections on admission, 6 showing *P. falciparum* and *P. vivax*, and 2 showing *P. falciparum* and *P. malariae*. The results in these cases are not discussed separately but are included under the different plasmodia.

Relapse rate

(a) *Vivax infection.*—Of 18 patients with *P. vivax* infection treated and kept under observation for a period of 5 weeks or more in the hospital, 6 showed clinical relapse of fever with parasites in the blood; one other patient showed parasites in the blood for one day only, and developed no fever. The interval between the cessation of treatment and the occurrence of relapse varied between 25 and 56 days, the actual intervals in these cases being 25, 26, 27, 42, 49 and 56 days.

It appeared that relapse was more common in those with a history of previous attacks of malaria with relapse than in the others with no such history. Of 6 patients who relapsed after one treatment, 4 had a history of previous relapses, whereas in 12 cases with no relapse after our treatment, the fresh infections numbered 10. Thus relapse appeared to be less common in fresh infection*.

To summarize: of 18 *P. vivax* infections during the period of observation varying between 5 and 10 weeks and averaging about 6½ weeks, 33 per cent relapsed. This figure is high and it probably does not include some late relapses, but it is little if any higher than figures given for similar studies of results of treatment with mepacrine or quinine.

(b) *Falciparum infection.*—Of 16 patients showing falciparum infection treated and kept under observation for a period of 5 weeks or more, none showed relapse of falciparum infec-

*This point is one not generally appreciated in studies of malaria relapse rates. Cases with already one relapse are likely to relapse again; they form a selected group, not comparable to a group of fresh infections.

tion although one showed an attack of vivax infection.

(c) *Quartan infection*.—The only case of quartan infection which responded well to treatment was kept under observation for only 3 weeks.

Work at the Narkeldanga Relief Camp

Seventy-five patients were treated with the assistance of the medical staff of the camp. All cases of active malaria with reasonably heavy infection seen during the period of study were treated, without any other selection. The conditions of the work were such that it was difficult or impossible to obtain accurate histories. The diagnosis of malaria however was accurate; the temperature records were kept by the medical staff of the camp; the daily blood examinations were performed by our staff. Many of the patients were in poor physical condition and, as will be seen later, some of them suffered from serious complicating diseases. The patients were kept under observation and had regular blood examinations made for a period of a month or more after the treatment had ceased. The dosage used was two tablets a day and proportionately less for children.

Of the 75 cases treated, 7 either did not complete the treatment or else could not be kept under observation and are therefore not considered here, 68 cases being left. Of the 68 cases, 32 showed *P. vivax* infection only, 24 showed *P. falciparum* infection only, and 12 showed mixed infections, 10 of these showing *P. vivax* and *P. falciparum* and one showing *P. vivax* and *P. malariae*.

Toxic effects.—Toxic effects such as nausea, vomiting, following the administration of the drug were slight and caused no serious difficulty, but as in the hospital series, some deaths occurred. In this series of 75 cases the deaths were 3. It was a striking fact that in all these three patients there were definite signs of disease of the respiratory tract; one had definite evidence of broncho-pneumonia, and the others had signs in the chest suggesting pulmonary tuberculosis, although thorough study of these cases was not possible. Nevertheless the fact that these deaths occurred, two on the fourth day of treatment and one on the sixth day of treatment strongly suggests that the drug contributed to the death, and further sug-

gests that the danger of toxic effects is increased in the presence of complicating diseases. Unfortunately post-mortem examinations could not be made in these patients, so detailed findings are not available.

Effectiveness of the drug in controlling the attack.—In all the 75 cases treated, including the three patients who died, the blood became negative in about the time indicated above in the hospital cases, and the malarial fever was controlled (although fever due to complications persisted). The results therefore corroborated those seen in the hospital cases and these results need not be discussed in detail. In *vivax* and *falciparum* infections results were excellent. The additional information provided by this series on relapse rate is of value.

Relapse rates.—Of 33 patients showing *falciparum* infection and kept under observation for several weeks, not a single one showed relapse of *falciparum* infection, but eight showed a recurrence of fever with *P. vivax* in the blood. The time of this recurrence of fever varied between 14 and 38 days after the cessation of treatment. It seems probable that most of these cases were really cases of mixed infection undetected before treatment. Some of these later fevers may have been due to fresh infections, for the work was mostly done in a camp in a highly malarious area in the middle of a malaria epidemic.

Of 42 cases of *vivax* infection treated and kept under observation, 12 showed clinical relapse and 6 showed scanty parasites in the blood but no fever, the parasites usually disappearing in a few days. The relapse occurred at intervals varying from 19 to 36 days after finishing treatment. Of the 30 patients showing no relapse, 22 were kept under observation for more than a month, most of them for periods varying between 5 and 7 weeks.

Summary and conclusions

The I. C. I. drug M 3349 has an action in malaria comparable to that of quinine and atebrin, the fever due to *P. falciparum* and *P. vivax* being promptly controlled and the blood becoming negative. In quartan infection however the effect was relatively poor.

Of 60 patients with *P. vivax* infection treated and kept under observation for a period of several weeks, 18 showed clinical relapse after intervals varying from 19 to 56 days, and 7 showed temporary recurrence of the parasites

in the blood with no fever. Thus the early relapse rate during this period of observation is 30 per cent, comparable with that usually seen after *P. vivax* infection treated with quinine or atebirin for a similar period.

Of 51 patients showing *P. falciparum* infection and observed for several weeks, none showed a relapse of falciparum infection, 8 showed a recurrence of fever with *P. vivax* in the blood; some of these are possibly cases of previously undetected mixed infection, but the possibility of fresh infection cannot be ruled out.

In persons who, apart from the malaria, are healthy and in reasonable physical condition, the toxic effects seen after administration of the drug, nausea and vomiting, etc., are slight and present no great difficulty. In persons with complicating diseases particularly of the respiratory tract, the danger of serious toxic effects seems to be greatly increased. In our present series of 106 cases among sick destitutes, 5 deaths were seen. Four of these were in patients with serious complicating diseases, but in these and in the fifth case it appears that the drug probably contributed to the causation of death. Toxic effects were first observed with the dosage of 0.6 gm. per day as recommended by the manufacturers, but they were not eliminated by the reduced dosage of 0.4 gm.; in fact, three of the deaths occurred on such a dosage.

The drug is of interest because it is apparently an entirely new chemical compound with a powerful antimalarial action, but in its present form its toxicity would appear likely to prevent its general use. Possibly some allied chemical compound may be equally or more effective and less toxic.

CEREBRAL MALARIA

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THIS paper is an analysis of 39 cases of M.T. malaria showing signs of involvement of the central nervous system. These cases are described under five groups according to the predominant symptom in the following table.

Discussion

Plasmodium falciparum sporulates in the internal organs, specially in those with a rich blood supply; hence the brain is frequently affected. Cerebral malaria is a great mimic of other diseases; it can simulate any acute

cerebral affection, e.g. meningitis; coma, encephalomeningitis. The pathological changes in the brain are not uniform and it is rash to formulate any specific relationship between them and the symptoms manifested. Fits are apparently an expression of anoxia of the cortical motor cells, leading to hyperexcitability and consequent discharge. The meningitic and encephalitic forms, in some cases, conform to a true type of meningo-encephalitis with punctiform hæmorrhages and direct evidence of inflammation with areas of necrosis. Thrombosis in the superior sagittal sinus is obviously not an unusual feature, though it has not been reported before; it gives no definite antemortem signs in cerebral malaria, headache, vomiting and meningitis signs being common to sagittal sinus thrombosis and cerebral malaria. The special features of sinus thrombosis, e.g. convulsions, bilateral hemiparesis, and vesical sphincter disturbances, were not present in any of the three cases.

The essential and immediate cause for cerebral symptoms appears to be a diminution of oxygen supply to the nerve cells. If the anoxia is of short duration, the damage is not severe and the patient recovers; if it is severe, the changes are irreversible and death or residual symptoms result. The anoxia may be brought about by—

(i) Blockage of capillaries by sporulating organisms and focal degeneration, by parasitized red corpuscles or due to toxic action of hæmzoin pigments causing cloudy swelling and degeneration of phagocytic cells. Capillary endothelial damage may produce pericapillary exudation and cerebral œdema, leading to increased intracranial pressure and cerebral anoxia.

(ii) Endothelial damage to venous capillaries, resulting in venous thrombosis and consequent obstruction to outflow from brain and cerebral anæmia, leading to cerebral anoxia.

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TABLE

Details of case	Symptoms on admission	Laboratory findings	REMARKS	Autopsy findings
<p>Group I. 8 cases seen, 4 fatal. Unconsciousness prominent, preceded by cerebral irritability or drowsiness. Associated features: hypernoea and other respiratory signs in 6, loss of jerks in 4, exaggeration of jerks with positive Babinski and sustained ankle clonus in 4; sluggish reaction to light in 4. Jacksonian fits, hyperpyrexia, and eye signs also seen. Intravenous quinine 6 grains 6-hourly was the treatment adopted. The following are the notes on the four fatal cases.</p>				
1 23 years, admitted in an unconscious state.	Unequal dilated pupils, deviation of eyes upwards and to right; jerks diminished, ankle clonus sustained, abdominal reflexes lost; bilateral indefinite plantar response present.	M.T. rings.	Pt. developed terminal hyperpyrexia and died.	Intense congestion of meninges; scattered cortical and sub-cortical hæmorrhages. Spleen and liver enlarged. Hæmorrhage in suprarenals. Brain and spleen smear showed M.T. parasites.
2 27 years, admitted with headache and drowsiness.	Headache and drowsiness deepened and jaundice appeared next as also petechial hæmorrhages on the skin.	Do.	Died in coma.	Petechial hæmorrhages on surface and in white matter of brain. An adherent ante-mortem clot in superior sagittal sinus. Endothelium of sinus thickened and desquamated. Brain and spleen smear showed M.T. parasites.
3 20 years, admitted in an unconscious state of two hours' duration.	Afebrile; pupils normal in size, not reacting to light.	Do.	Died shortly after admission.	Do.
4 21 years, admitted in an unconscious state.	Temperature 105.6°F.	M.T. rings. C.S.F. clear under normal pressure.	Died next day.	Brain oedematous and congested; adherent thrombus in superior sagittal sinus. Advanced degeneration in parenchyma, almost like infarction necrosis. Virchow-Robins spaces dilated with remain of contracted blood vessels. Larger vessels show thrombus formation and epithelial desquamation. Spleen very congested with loss of architecture; dark brown malarial pigment seen.
<p>Group II. 14 cases seen, 1 fatal. Meningitic signs predominant; headache, delirium and restlessness were present in all the cases as also positive Kernig's sign and neck rigidity. C.S.F. clear, under pressure. Responded to initial 1 or 2 doses of intravenous quinine and routine antimalarial therapy. The following are the notes on the fatal case.</p>				
5 24 years, admitted for fever with rigor.	After 9 days had a sudden rise of temperature, became semi-comatose, Kernig's sign positive; neck rigidity.	M.T. rings.	Had retention of urine and died.	Congestion of meninges; marble-sized blood clot in right occipital lobe, with destruction of nerve tissue around. Smear positive for M.T. Cerebral and cerebellar parenchyma showed degeneration with areas of necrosis; inflammatory cells forming a collar along meningeal layers.
<p>Group III. 3 cases seen, none fatal. Epileptiform fits predominant; 2 cases had fits along with the onset of fever and the third developed fits 6 days after onset, during treatment. The notes of a typical case are given below.</p>				
6 25 years, admitted with dysenteric symptoms. Unconscious for two minutes, then rigor and high temperature.	Fit 5 days later, sudden onset, deep slow breathing, absent, corneal reflex, light reflex slow, eyes deviated. Ankle clonus positive and sustained. Plantar response flexor.	Both B.T. and M.T. parasites.	Responded to treatment. Spleen not palpable.	

TABLE—*concl'd.*

Details of case	Symptoms on admission	Laboratory findings	REMARKS	Autopsy findings
<i>Group IV.</i> 10 cases, none fatal. Mental symptoms predominant; slowing of cerebral functions with poverty of ideas in 8, loss of memory in 4, acute delirious mania in 6, aberrant behaviour in 6, partial aphasic phenomena in 2. Notes on 3 typical cases are given below.				
7 30 years, admitted for abnormal behaviour.	Temperature normal, perception good; dazed state.	No malaria parasites but only pigments.	Responded to antimalarial treatment.	
8 16 years, admitted in coma.	Temperature 101°F. Kernig's sign plus; neck rigidity plus; C.S.F. under pressure and tinged with blood.	M.T. rings.	Responded to antimalarial treatment in about a fortnight.	
9 20 years, admitted. Found unconscious on road.	Conscious but drowsy. Temperature 97°F., pulse 80, respiration rate 12. Kernig's sign positive; no neck rigidity. Tendon jerks lost; plantars flexor.	M.T. rings. C.S.F. normal.	Responded to antimalarial treatment.	

Group V. 4 cases seen, none fatal. One had 108.6°F. and was left with neurological sequelæ, probably due to the effects of the high temperature on the nerve cells.

FEVER IN A HYPER-ENDEMIC MALARIAL AREA

A CRITICAL ANALYSIS OF 2,913 CASES

By T. A. A. HUNTER, M.B., B.Chir., M.R.C.P.

COLONEL, R.A.M.C.

Commanding an Indian Malaria Forward Treatment Unit

'FEVER' is the small change of medicine in the tropics. Under civil conditions familiarity breeds contempt to such an extent that the great majority of cases are self-treated or, at the best, dosed without accurate diagnosis by the doctor. Even in the Army where some form of hospitalization is the rule, uncritical and unscientific management of minor fever cases is all too common. The fact that the majority of tropical fevers are strictly self-limited or respond symptomatically to minimum doses of anti-malarial drugs is apt to cloak the unsatisfactory nature of this attitude. It results, however, in the currency of a great variety of clinical impressions with regard to various aspects of the diagnosis and treatment of fevers, and a dearth of really authoritative information based on the analysis of adequate material. In this paper nearly three thousand consecutive cases of fever are analysed with a view to providing answers to some of the commoner questions.

The cases were all treated in one of the most highly malarious areas of the Assam/Burma border, in the height of the transmission season. All the sick arriving at the centre in question were diagnosed at a central distribution room. From this distributing centre this unit received up to a capacity all cases of fever, British and Indian, in which no definite diagnosis had been made. As well as these, diagnosed cases of malaria were received, though these were relatively few in number. On this basis it is considered that the series may be regarded as a fair sample of not yet diagnosed fevers from the military population of the area.

Non-malarial fevers and clinical malaria

There are two schools of thought about the diagnosis of non-malarial fevers in a hyper-endemic area. One school holds that in such an area, particularly if suppressive treatment is widely employed, every case of fever should be regarded and treated as malaria, unless some other diagnosis is at once apparent, quite irrespective of negative findings in the blood. The second school holds that specific treatment should be withheld until and unless the parasite is demonstrated.

In India generally there are found a large number of short non-specific, non-malarial fevers which figure variously in hospital

statistics as dengue, sandfly fever, pharyngitis, or more honestly, 'pyrexia of unknown origin'. *Prima facie* there seems to be no good reason why these should not also be common in the highly malarious areas. For this and other reasons the approach to this series was along the lines of the second rather than the first school. A working rule was made that at least four blood examinations should be made before specific treatment was started on clinical grounds. If four negative results had been obtained and the case was still clinically suggestive, treatment was started tentatively and only if this therapeutic test proved positive was a diagnosis of clinical malaria admitted. There were, however, a small number of cases admitted with the diagnosis of clinical malaria having already started treatment elsewhere. There did not appear to be any alternative to carrying on the treatment in these cases to the conclusion of the course.

On the basis of these diagnostic criteria, the following are the figures for the series :—

	British	Indian	Total
Proved malaria ..	643	1,563	2,206 (76%)
Clinical malaria ..	41	45	86 (3%)
Not malaria ..	177	444	621 (21%)

Let us first examine the cases recorded as being non-malarial. It is convenient to classify them in four groups.

Group 1.—(40 per cent) comprises cases in which a definite diagnosis other than malaria was made, which adequately accounted for the 'NYD fevers' picture on admission.

Group 2.—(25 per cent) comprises cases who exhibited no fever or other symptoms after admission, though often giving a history of fever or, at any rate, subjective evidence of fever, before admission.

Group 3.—(30 per cent) had a rise of temperature on admission which settled without treatment within thirty-six hours and did not recur before discharge four days later.

Group 4.—(4 per cent) exhibited a remittent type of fever which settled without treatment within four days and did not recur there after before discharge four days later.

The cases in groups 1 and 2 can probably be accepted as unquestionably non-malarial. About the cases in groups 3 and 4, however, there is more room for argument. In an

attempt at a direct answer, a follow-up on a small scale was carried out on the group 4 cases. Ten of these cases were given follow-up postcards. Seven of these replied. Six were fit and on duty one month after discharge, one was admitted to hospital with benign tertian malaria ten days after discharge, and three failed to reply. As far as it goes, this evidence tends to support the rejection of malaria as a diagnosis. These cases were not receiving suppressive treatment, and had their illness been, in fact, malaria, the majority of them would have been expected to declare themselves in the ensuing month. The actual incidence is no higher than would be expected in any similar group of men in this area.

Now let us turn to the cases recorded as 'clinical malaria'. A quarter (24 per cent) of these were diagnosed as such after admission. This figure amounts to rather less than one per cent of the whole series. The remaining 76 per cent of the recorded clinical malaria cases were admitted as such. A study of these transferred cases threw considerable doubt on the justification for the diagnosis in the majority of them. None of them gave any history of symptoms or signs such as would make early treatment imperative.

At the most, only one blood examination had been made, and treatment had frequently been started before the result of this blood slide was obtained. Five cases had definite pneumonia and five follicular tonsillitis on admission, and there is little doubt that these diseases and not malaria was the cause of their fevers. Taking all the factors into consideration, history, condition on admission, reaction to treatment, it was considered in retrospect that, at the most, only about a sixth of these cases were at all likely to have been cases of malaria. It will be seen then that 'clinical malaria' amounts to a very small proportion of the total cases of fever, if the not unreasonable criteria which we have laid down for its diagnosis are accepted.

Before going on to the discussion of the case for and against the diagnosis of clinical malaria, there is one other point to be taken from the figures. It is often argued that the use of suppressive treatment vitiates the accurate diagnosis of malaria. In the present series some two-thirds of the British troops had been receiving suppressive

treatment whereas only a negligible number of the Indians had done so. Despite this discrepancy the proportion of non-malarial cases in the two groups is almost identical : 20 per cent British and 22 per cent Indian.

Malaria is one of the few diseases in which an absolute diagnosis is possible during life by relatively simple means. A 'clinical' diagnosis is, therefore, scientifically indefensible. It has, however, many supporters on the grounds of expediency. One of the commonest arguments put up in its favour is to the effect that to wait for a positive blood slide before starting treatment will commonly prejudice the outcome of the severe case. It is difficult to subscribe to this argument in the light of experience. Severe types of malaria are relatively uncommon, 2.4 per cent in this series, and among them the fulminant forms are rare. The argument at the best is only applicable to a very small fraction of one per cent of all cases. The taking and examination of a thick drop of blood takes only a few minutes and evidence is produced under a later heading of this paper that the parasite is apparent in between 80 and 90 per cent of first slides from all cases subsequently proving to be malaria. In the severe cases of this series, it has been found that the parasites are particularly plentiful in the peripheral blood and no evidence has been seen in support of that bogey man of the medical officer, the cerebral case with persistently negative blood slides. This opinion has been supported by a pathologist who has seen many hundreds of severe cerebral malaria cases. It is, therefore, argued that on the grounds of saving life, treatment need only be given 'clinically' when there are no facilities for blood examination and then only to the rare case that exhibits fulminant symptoms.

Another argument put forward claims that the missed case of malaria will frequently lose his symptoms for a short while and then relapse with a fulminant attack of the disease. Absolutely no evidence has been found in support of this theory. In point of fact it is difficult to see how such evidence could be produced. The thick-drop method of blood examination is extremely sensitive. It will commonly detect the sub-clinical concentration of parasites present in the blood of individuals taking suppressive treatment and it is only reasonable to presume that careful and

repeated examinations will always reveal malaria parasites if they are present in sufficient numbers to cause symptoms. This particular argument savours rather of the 'malaria hysteria' that is apt to affect workers in a very highly endemic district.

On the other side of the question, too easy a resort to the diagnosis of clinical malaria has a very real danger. It brings treatment into the relatively easy realm of routine, and subconsciously is apt to relieve the doctor of the responsibility for further diagnostic effort. The results of this are all too apparent. In this series alone, five cases of pneumonia have been missed probably largely through their being labelled clinical malaria, and even more serious lapses are familiar to most workers in tropical medicine. In those few cases where this term has got to be used, it must be recognized as a label and not a diagnosis, and its tentative nature must be kept always in the foreground.

Apart from this danger, there is a practical objection of some consequence particularly in military practice. A case of malaria is absent from duty for a period of fifteen days, whereas the average non-malarial fever patient is fit well within a week. In other words there is a saving of at least one man-week per case with the latter as opposed to the former diagnosis. On this basis, if the cases in groups 2 and 4 above had been regarded as clinical malaria instead of non-malarial, there would have been an additional loss of 220 man-weeks duty. This series represents only a small fraction of all the cases in the Army, and it must be apparent that this constitutes an important point in the conservation of man-power. The standards of malaria diagnosis vary enormously, and it would be by no means unthinkable for all the cases mentioned to have been regarded and treated as clinical malaria.

There is one final point. A fortnight to three weeks in hospital undergoing malaria treatment has obvious advantages over the dangers and discomforts of front line soldiering. There are many troops, both British and Indian, who are not averse to availing themselves of these advantages even under false pretences. It is easy to present almost any symptoms or none at all in the form of a history that will suggest malaria. This form of malingering though not widespread, undoubtedly exists, and it can only be minimized

by maintaining the highest standards of objectivity in the diagnosis of malaria.

Species distribution

The distribution of species types in the series is set out in the following table. The 'thick drop' was the routine method of blood examination used. It cannot therefore be claimed that the table represents one hundred per cent accuracy. It is thought however that the percentage error is low and that for all practical purposes the picture is a true one.

	M.T.	B.T.	Qt.	Mixed
British troops ..	30%	64%	1%	6%
Indian troops ..	43%	47%	1%	9%
Combined ..	39%	52%	1%	8%

The figures as a whole are only of interest as showing the incidence of the various species types in this particular area at this particular season of the year. There is, however, one point

Indian troops to infection by *P. vivax* which is the commonest infecting agent in the parts of India where most of them have been brought up. Such a differential immunity would result in a higher proportion of M.T. infections among Indians as opposed to British. Here it must remain a speculation but it is a point that is worth following up as the whole question of the immunology of malaria is somewhat of a neglected study.

Attack incidence

In attempting to arrive at the attack incidence in a series such as this, one is faced with an immediate difficulty. The soldier at the present time carries no personal medical history, and therefore reliance has to be placed entirely on the man's own statement. British troops can, as a rule, give fairly reliable information as to the number but not the exact nature of their previous attacks. In the case of Indian troops, even the number is at the best an approximation. Under these circumstances, the only figures that can be produced are the number of times that any given man has had malaria previously. These figures for this series are set out in the following table:—

			1ST ATTACK			2ND ATTACK			SUBSEQUENT		
			M.T.	B.T.	Qt., M., Cl.	M.T.	B.T.	Qt., M., Cl.	M.T.	B.T.	Qt., M., Cl.
British	55%	54%	50%	10%	18%	18%	27%	36%	32%
Indian	44%	40%	44%	34%	33%	34%	22%	27%	22%

of some interest that comes out on analysing them. Among Indian troops the incidence of M.T. and B.T. infections is almost identical while among the British troops the B.T. incidence is almost double that of M.T. Almost certainly the explanation lies in the fact that a considerable proportion of the British troops were receiving suppressive mepacrine while only a negligible number of Indians received it. This evidence therefore strongly supports the theory that mepacrine is more effective against *P. falciparum* than against *P. vivax*. It is understood that this fact has been clearly demonstrated in recent experimental studies in Australia. There is also another factor which may play a part in this discrepancy. It is possible to imagine a certain amount of acquired differential immunity on the part of

Apart from the limitations of the data outlined in the last paragraph it is obvious that further information is necessary if any useful conclusions are to be drawn; the movement of fresh troops into the area, the average length of stay, etc. These facts were not available, and therefore these figures serve only to demonstrate once again the truism that malaria is essentially a recurrent disease. More than half of the cases treated had had at least one previous attack. It is quite impossible however on the facts available to hazard even a guess as to how much of this recurrence is due to relapse and how much to reinfection.

The spleen in malaria

The findings as to enlargement of the spleen are set out in the following table.

	NOT ENLARGED			TRANSIENT ENLARGEMENT			PERSISTENT ENLARGEMENT		
	M.T.	B.T.	M., Qt., Cl.	M.T.	B.T.	M., Qt., Cl.	M.T.	B.T.	M., Qt., Cl.
British	76%	74%	71%	22%	24%	26%	2%	2%	3%
Indian	59%	58%	57%	15%	18%	16%	26%	24%	27%

The fact that in nearly two-thirds of all cases the spleen was not palpable is rather contrary to the usual textbook teaching on malaria. Many will agree however that it conforms to current clinical experience in military practice. The higher rate of splenic enlargement among Indians as opposed to British troops is also in accordance with experience, and is undoubtedly, due to the remote rather than to the recent past. It will also be noted that the tendency to splenic enlargement does not appear to vary significantly with the species of the infection.

There is a common tendency to relate enlargement of the spleen with the multiplicity of attacks. An examination of the figures in this series does not support this view. The following table is taken only from the records of the British troops as in the case of the Indian the history was thought to be too uncertain for reliable data.

	Not enlarged	Transient	Persistent
First infections ..	75%	20%	5%
Subsequent infections	72%	24%	4%

It will be seen that the rates are almost identical, so that it appears that some factor other than the number of attacks governs the enlargement of the spleen. This is borne out by the clinical observation that it is commonplace to see patients who give a history of very numerous attacks of malaria and yet show no enlargement of the spleen. In actual fact, it is suggested that splenic enlargement depends on the time for which a given attack of malaria is allowed to go untreated. It has been aptly stated that 'the spleen is the graveyard rather than the nursery of the malaria parasite.' Enlargement can, therefore, be expected to take place when the spleen has to exercise its parasiticidal function unduly long owing to the infection being unchecked by specific treatment. British troops almost invariably receive treatment very soon after the first development of

symptoms and, for that reason, the rate of persistent splenic enlargement among them is very low.

Suppressive treatment in many cases probably permits the persistence over long periods of a sub-clinical number of parasites in the blood. It would, therefore, be expected, if the above view is correct, that patients who have been receiving suppressive treatment will show a higher rate of splenic enlargement than those who have not received this treatment. The figures from this series illustrate this point and are given in the following table:—

Cases on suppressive treatment.	27% showed some splenic enlargement.
Cases not on suppressive treatment.	18% showed some splenic enlargement.

From the point of view of the diagnosis of active malaria it may be stated that an enlarging tender spleen is of far greater significance than a mere static enlargement however marked.

Blood slide technique

The standard practice for this series has been the examination of a thick drop stained by Simeon's method. This technique has proved entirely satisfactory. It is quick and for a thick-drop method gives an extraordinary degree of differentiation of species. Although a thin film was taken on the same slide in each case it was only very rarely necessary to stain this for confirmatory purposes.

At this point it is worth calling attention to a matter that is very often forgotten and which has a very important bearing on the efficient handling of malaria cases. If the temptation to resort to the diagnosis of clinical malaria is to be minimized, blood examinations must be carried out with the utmost possible despatch. Good laboratory technique is essential but the best technique will not compensate for poor slide-taking or for delays in taking the slide to the laboratory and the report to the ward. This is a fairly simple administrative problem

but it is surprising how often it is neglected, with the consequence that twenty-four hours elapses before the report on the first slide reaches the ward. In all malarial areas, facilities for the taking of blood slides should be provided in the admission room and a twenty-four-hour laboratory service should be available.

The following table illustrates that with a thick-drop technique there is seldom any need for the examination of large numbers of slides from any one case.

		1st slide	2nd slide	3rd slide
British	81%	8%	11%
Indian	90%	6%	4%

Effect of suppressive treatment on blood slide

Among the British troops, although a considerable proportion of them had been receiving suppressive treatment more than 80 per cent of first blood slides were positive. It is evident therefore that the effect of this treatment on microscopical diagnosis is not profound. In the majority of cases which had had this treatment, it had been continued until twenty-four to thirty-six hours before the blood slide was taken on admission to hospital, having been omitted during the transit period. When the first slide was negative, a second was taken as a rule within twelve hours of the first. On the aggregate of the first and second slide results, there is not a great deal of difference between the British and Indian figures in the above table. The conclusion appears to be justifiable that suppressive treatment slightly reduces the probability of getting a positive microscopic diagnosis while it is actually being taken but that this effect rapidly wears off. In practice there should not be any serious diagnostic difficulty.

The following table showing the differential figures in British troops receiving and not receiving suppressive treatment are also pertinent.

	1st slide	2nd slide	Subsequent slide
On suppressive treatment.	77%	11%	12%
Not on suppressive treatment.	83%	9%	8%

Diagnostic aids: Adrenalin injection

Current opinions vary on the value of adrenalin injection as a provocative measure in the diagnosis of malaria. In the latter half of the present series of cases it was used as a routine before taking the fourth slide, if three had previously proved negative and the diagnosis was still in doubt. Seventy cases in all received it and in seven a positive finding was obtained after and, presumably, as a result of its use. Its value is greater than these figures at first suggest, in that a proportion of them were subsequently proved to be other than malaria apart from the presumption that all the negatives were non-malarial. The method appears materially to increase the chances of a definite microscopical diagnosis and is considered worth using as a routine in doubtful cases. There was some evidence that it is most likely to give results when some degree of splenic enlargement is present.

Sternal puncture

This investigation was carried on twenty persistently negative cases who were still clinically suggestive. In none of them was the parasite found in the smear from the marrow. The procedure is simple and almost wholly unobjectionable but it does not appear to have any useful place in the diagnosis of malaria.

Splenic puncture

Splenic puncture has been performed on three negative cases which had persistent pyrexia. The first of these gave a negative result and the fever subsequently subsided. The second, which had also previously had a negative sternal puncture, showed L.D. bodies in the smear and no accompanying malaria parasites. The third case, which had very numerous negative blood slides, showed both *P. vivax* and *P. falciparum* in the spleen smear. Only this last case showed any ill effects from the puncture. There was slight pain in the splenic region with evidence of mild peritoneal irritation which lasted for a day. Although these symptoms were not such as to cause serious alarm, it is considered that this method should be used with caution in probable cases of active malaria. It does not seem to be suitable for use as a routine diagnostic method.

Severe types

The incidence of severe types of malaria in this series was unexpectedly low. Only eight British cases and four Indians were considered to have cerebral involvement, and only three of these gave cause for real anxiety. There were no examples of algid malaria and no deaths.

Two factors are thought to have played a part in this low incidence. In the first place the utmost care was taken to ensure rapid and accurate microscopical diagnosis. The great majority of cases had been diagnosed and had treatment started within an hour or two of admission. Secondly, it was made a routine practice to give an immediate dose of quinine intravenously to all M.T. cases which either exhibited symptoms of any degree of severity or whose blood slide was found to be 'heavily infected'. This routine was initiated as a result of experience with the first of the British cerebral cases. This man was admitted one evening with very ordinary symptoms of fever. His thick drop was found to be heavily infected with *P. falciparum* and he had ten grains of quinine by mouth immediately. This dose was repeated next morning and at midday he appeared to be running a normal course. The medical officer who came in the early afternoon to give him his third dose found him unconscious and it required energetic intravenous therapy over several days to pull him round. This case illustrates on the one hand the occasional volcanic nature of malignant malaria and on the other hand the unreliability of the absorption of orally administered drugs.

The temperature chart

For the purpose of studying the temperature chart, an analysis was made of the pure M.T. and B.T. infections among the British troops.

The temperature charts met with can be classified under three types. Type 1 showed no rise of temperature after admission. This probably represents the cases that were admitted at the end of a paroxysm of fever and in which the next rise was absorbed by the institution of treatment. Type 2 exhibited an intermittent type of fever with a quotidian or tertian periodicity, more than two peaks being extremely rare and limited to the cases where diagnosis was delayed. Type 3 gave a sustained fever settling at least before the start of the fifth day of treatment. Type 4 had a similar sustained

type of fever which was maintained up to the fifth to seventh day of treatment. The relative incidence of these four types was as follows:

Type 1	..	35%
Type 2	..	35%
Type 3	..	25%
Type 4	..	5%

Types 1 and 2 represent the classical type of malarial fever and it is apparent that they definitely preponderate. As is well known however the less typical form represented by types 3 and 4 is by no means uncommon.

The following figures show that there is a distinct tendency for this latter type of chart to occur more commonly in M.T. than in B.T. infections:

Types 1 and 2	..	24% M.T.	76% B.T.
Types 3 and 4	..	43% "	57% "

The well-known tendency for the classical type of chart to be commoner in relapses than in fresh infections is also well shown by the following figures :

Types 1 and 2	..	55% fresh	45% recurrences
Types 3 and 4	..	72% "	28% "

A study of the behaviour of the temperature charts also demonstrates the degree to which the outward and visible signs of malaria are controlled by a minimum of specific treatment. Fever is, in most cases, the only objective clinical evidence of active malaria. Among these cases, 76 per cent remained apyrexial after the completion of the second day of treatment. Twenty per cent remained apyrexial after completing four days' treatment, and only 4 per cent were pyrexial up to the end of their seven-day course. The significance of this fact is that after two or three days' treatment there is, as a rule, no objective clinical means of telling whether or not treatment is actually being given. This emphasizes the need for the greatest possible care in the supervision of treatment. There are inevitably a number of patients who try to evade treatment, and the ease with which the drugs concerned can be disposed of at fantastic prices puts considerable temptation in the way of subordinate staff to abet this evasion. Apart from this deliberate evasion, in dealing with large numbers, it is quite easy to miss individuals unless a watertight system is in use, and there are relatively few soldiers that will go out of their way to seek treatment. The regular testing of

random samples of urine for absorption of the drugs serves as a useful check. The occurrence of more than a very occasional negative indicates that the system wants overhauling. Experience with this series has shown that the most extreme care must be taken if a hundred per cent of cases are to be fully treated and that the precautions officially advocated from time to time are practical necessities and in no way 'eyewash.'

Suppressive treatment

Experience with suppressive treatment has been on the surface of things contradictory. On the one hand approximately one-half of the British patients admitted with malaria were allegedly on a suppressive dose of one tablet of mepacrine daily and only a half of these would admit on cross-examination that there had been any irregularity in the administration of this dose. On the other hand the experience with the unit's own personnel was directly contrary to this. For two months the malaria rate among the Indian personnel of the unit was in the region of two hundred per thousand per fortnight. They were then put on suppressive mepacrine and in the next two months there were only three cases of malaria, in all of whom there was some such element as leave that could be expected to interfere with the regularity of dosage. The numbers involved were approximately two hundred. There does not appear to be any doubt that mepacrine given regularly in the doses indicated is absolutely effective in suppressing malaria. The difficulty lies in ensuring absolute regularity of administration. It is relatively easy in a medical unit organized primarily for the administration of anti-malaria treatment, but by no means so in a non-medical unit in the field. Even here it is possible but it requires a degree of organization and of discipline that has not as yet been devoted to it.

Points in treatment.—As had been already indicated, random sampling of urines for the presence of quinine and mepacrine has been carried out as a routine. The results of these tests show that the Tanret-Mayer test normally becomes positive after two to three ten-grain doses have been given, and the mepacrine test after three to four tablets of mepacrine. Subject to these limits, only very rarely was a negative result obtained. A study

of these occasional negatives suggests that constipation plays an important part in interfering with the absorption of both quinine and mepacrine. There is therefore some justification for the rejected claim that calomel has a specific effect on the malaria parasite. Although this is not strictly true, the use of a preliminary purge is an essential adjuvant to specific treatment.

Very little real difficulty was experienced on the score of vomiting. It is considered that the vomiting of quinine is almost entirely under voluntary control. Firm handling and immediate re-dosing up to three or four times will cure almost all cases. If these cases are not thus firmly handled, there is a danger of the practice reaching almost epidemic proportions in a ward.

Free and early use of intravenous quinine has been resorted to for the reasons previously outlined. With slow injection of the standard ampoule containing six grains in ten cubic centimetres of normal saline, no untoward symptoms were met with in a large number of cases. It is difficult to understand the fear of this method which is entertained in many circles.

Current Army regulations reduce the treatment of malaria to an unalterable routine consisting of sixty grains of quinine over two days, fifteen tablets of mepacrine over five days and then after two days' rest fifteen tablets of pamaquin over five days. There are therefore no data on which to discuss the merits of different forms of treatment.

Treatment of resistant malaria

So specific are quinine and mepacrine in the destruction of the asexual forms of the malaria parasite that apparent 'cases' of resistance to these drugs are often dismissed as being due to faulty administration or failure of absorption. While agreeing that true drug resistance is extremely rare the following case history is submitted as evidence that it can exist.

An Indian was admitted on 30th April with six days' history of intermittent fever and rigors. He admitted to an attack of malaria two months previously. On 1st May his blood slide was found to contain *P. vivax*, and he started a routine course of treatment. This proceeded ordinarily until 14th May, when he had a rise of temperature and a rigor. These were repeated on 15th May and on 16th May *P. falciparum* was found in his blood. A second course of treatment was started. Urine test on 17th May and on 21st May confirmed the absorption of quinine and mepacrine

respectively. There was, however, a very slow response to treatment and the temperature did not return to normal until the last day of mepacrine treatment, 22nd May. The spleen had been hard and palpable, two fingers below the costal margin on admission and up to this point had remained unchanged. On 26th May, four days after the conclusion of his second mepacrine course the temperature started to swing again and the spleen to enlarge and become tender. Daily blood slides and a sternal puncture smear were negative but no non-malarial cause could be found for the fever. On 30th May a splenic puncture was done and the smear showed growing forms and gametocytes of *P. vivax* and tenue forms and crescents of *P. falciparum*. On 1st June a course of quinine by Sinton's alkali method was started and absorption was confirmed by urine tests on 5th, 7th and 9th June. The temperature was very slow to settle and a culture taken on 8th June still grew *P. falciparum*. The quinine course was continued until 12th June. This time, apparently treatment had at last proved successful. The temperature remained normal and the spleen had returned to its original state. A second culture taken on 13th June was negative.

It is difficult to explain the chain of events in this case without postulating a quinine and mepacrine-resistant strain of the parasite. The recurrent attacks might conceivably have been due to reinfections, but this would not explain the persistence of the parasite in the blood after eight days' controlled quinine therapy.

Relapse

Probably the biggest problem in the treatment of malaria is the prevention of relapses. The control of an individual attack rarely presents much difficulty and can be achieved by almost any combination of quinine and mepacrine in a maximum of a week. To justify a longer course of treatment than this it seems reasonable to require evidence that this longer course minimizes the tendency to relapse. Under present military conditions it is difficult to see how this evidence can be accumulated. In practice no record is kept of the individual soldier's medical history, and his own statement is apt in many respects to be unreliable. Also in the majority of cases it is impossible to distinguish between a relapse and a reinfection. This latter point was well seen in the present series. Some score of the cases observed were known to have had a second attack of malaria either before or just after discharge. In a number of these cases, blood examination showed the second attack to be due to a different species of parasite to the first thus proving that they

were, in fact, reinfections.* There is no means of telling how many of the remainder were reinfections with the same species. It is well known that none of the drugs used in the treatment of malaria has any effect on sporozoites. It is therefore obvious that sporozoites introduced during the first week of treatment when quinine and mepacrine are being given have every opportunity of developing in the second week unhampered by the pamaquine, which is the sole medicament during that stage. Reinfection during a course of treatment is therefore a theoretical possibility and has been shown to occur in practice. It is reasonable to assume that it accounts for a major proportion of immediate second attacks when malaria cases are treated as these were in a highly-infected area.

If any advance is to be made in settling the question of relapse after treatment two things are essential. Firstly, a universal follow-up and system of personal medical histories and, secondly, the treatment of a sufficiently large controlled series in a non-malarious area and their retention in that area for a period after treatment. Without these requisites the matter must inevitably remain one of pure speculation.

Conclusion

In conclusion acknowledgment is due to the entire medical staff of the unit where these cases were treated and particularly to Captain J. N. Fairley, R.A.M.C., and Captain A. Sen Gupta, I.A.M.C. Without their very able assistance this paper could not have been written. Acknowledgment is also made to the Director of Medical Services, Alsea, for permission to publish this paper.

SOME OBSERVATIONS ON KRUKENBERG TUMOUR OF OVARY

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A word of apology is needed in introducing any discussion on Krukenberg tumour, considering how infrequently the condition is recognized. But we agree with Masson (1934) that it is not so rare as is usually supposed. Shaw (1932) showed an incidence of 1-per cent in his series of cases, but Dieckmann collected

* This does not follow in all cases. Mixed infections are often undetected by routine examinations, particularly *P. vivax* in a case in which *P. falciparum* alone is detected on admission and during treatment; the latent vivax infection frequently relapses while the falciparum infection does not.—Editor.

TABLE

Details of patient	History	Clinical examination	Laboratory examination	Operation	Pathological report	Microscopic examination	Results or operation and remarks
1 51 years, nullipara. Rapidly growing tumour in abdomen for 6 months.	Melæna 8 months ago. Marked general weakness.	Patient undernourished. Free fluid present in abdomen. Hard, irregular mobile tumour growing from pelvis. Uterus pushed back by tumour.	Nil abnormal.	Double ovariectomy, total hysterectomy and bilateral salpingectomy. Pyloric growth present.	Both ovaries nodular, irregular in shape, typical indentations. Surface glistening and containing small cysts. Left— $7\frac{1}{2} \times 3\frac{1}{2} \times 2\frac{1}{2}$ inches. Right— $4 \times 2\frac{1}{2} \times 2$ inches.	Cellular tissue stroma increased and shows groups of large cells with finely granular protoplasm, staining intensely for mucus. Nuclei eccentric and 'signet-ring' like. Also found in tube walls and mucous membrane folds.	Carcinoma of pylorus treated with 10 exposures of deep x-rays. Nine months later recurrence and death.
2 48 years, primipara. Tumour in abdomen for 4 months.	Periods prolonged; profuse and painful, for 6 months.	Marked weakness and debility. Free fluid in abdomen. A mobile, irregular hard tumour was rising from pelvis 2 fingers above umbilicus pushing uterus anteriorly and to the right.	Moderate degree of anaemia and leucocytosis.	Tumour was growing from left ovary, right ovary enlarged and cystic. Total hysterectomy, bilateral salpingectomy, and left and right oophorectomy.	Left ovary tumour $7\frac{1}{2} \times 5\frac{1}{2} \times 3$ inches oval, partly cystic and partly solid; solid portion irregular and furrowed. Cystic areas also in tumour. Right ovary—only few serous cysts. Tubes elongated and hypertrophied. Uterus normal.	Appearance of cellular tissue stroma and 'signet-ring' cells.	Deep x-ray given, patient discharged after 21 days. She was free from any symptoms for 5 years afterwards.
3 45 years, 8th para. Tumour in abdomen for 8 months.	Last pregnancy 17 years ago. Periods regular. Dull pain in left iliac fossa recently.	Abdomen distended; tumour rising above umbilicus to left. Marked ascites. Vaginal mucous membrane prolapsed.	Nil abnormal.	Laparotomy. Blood-stained free fluid present. Tumour growing from left ovary and twisted. Right ovary contained cysts. Stomach contracted. Pyloric region contained growth; lymph glands enlarged. Secondary deposits in bladder, bowel and omentum. Bilateral ovariectomy and salpingectomy.	Right ovary almond-sized; small follicular cysts present. Left ovary tumour, $7\frac{1}{2} \times 4\frac{1}{2} \times 3$ inches; surface glistening, irregular and nodulated; partly solid and partly cystic; degeneration in solid portion.	Typical picture of Krukenberg tumour in solid portion of tumour. Cystic portion showed pseudomucinous cyst-adenoma.	Deep x-ray given and patient discharged on the 23rd day.
4 26 years, 3rd para. Rapid swelling of abdomen and pain for 3 months.	Last child 2½ years ago. Periods regular. Vomiting and occasional diarrhoea.	Free fluid present. Nodular irregular tumour rising from pelvis to umbilicus, not mobile. Uterus normal and pushed forward filling pelvis. Small nodular thickenings in posterior pouch.	Definite anaemia and leucocytosis.	Tumours hard, bilateral involving ovaries. Tubes congested and elongated and adherent. Bladder wall infiltrated. Stomach sp. pyloric region contracted and hard. Lymph glands enlarged. Ovarian tumours and tubes were removed.	Both tumours hard, irregular and lobulated. Left 3×2 inches waxy, degenerated and contained small cysts. Right— $3 \times 1\frac{1}{2} \times 1\frac{1}{2}$ inches. Left— $4\frac{1}{2} \times 3\frac{1}{2} \times 2\frac{1}{2}$ inches.	Cellular connective tissue stroma with large cells, etc., as in case 1. Tubes contained typical cells in wall.	Died 7 days after operation.

5	40 years, 7th para. Rapid painful swelling of abdomen and discomfort for 8 months.	All confinements normal, periods regular. Occasional indigestion and vomiting.	Nodular and hard tumour rising above umbilicus. Small hard masses in epigastrium and right hypochondrium. Uterus normal. Tumour rising from pelvis not mobile, left larger.	Exploratory laparotomy. Larger left ovary removed. Right ovary adherent. General peritoneal carcinomatosis with growth in pyloric region.	Tumour irregular and solid. Some areas of adeno-carcinoma; stromal reaction and 'signet-ring' cells present (figure 1).	Deep x-ray given and patient discharged after 17 days. Much improved 10 months later.
6	35 years, one child 9 years old. Rapidly growing swelling in abdomen for 5 months.	Periods scanty but regular. General weakness, indigestion for 7 months.	Fluid thrill and shifting dullness in abdomen. Hard irregular, mobile swelling growing from pelvis. Uterus enlarged, hard and retroverted. Moderate cystocele and rectocele.	Ovaries enlarged with hard and nodulated tumours. Double ovariectomy, total hysterectomy, and bilateral salpingectomy. Stomach shrunken. Retrogastric glands enlarged.	Left—4 × 3½ × 2 inches. Right—4½ × 2 × 2 inches. Typical indentations (figure 2) small cysts. Fundus of uterus showed small fibroma submucous.	Cellular tissue stroma and 'signet-ring' cells (figure 3). 300 c.cm. whole blood transfusion. Advised x-ray therapy.
7	26 years, nullipara. Nodular swelling in abdomen for 12 months.	Periods regular, but amenorrhoea for 5 months. Pain in lower abdomen and discomfort after taking food.	Anemic. Irregular tumours in epigastrium and right hypochondrium; hard tumours filling iliac fossae, pouch of Douglas, and pelvis, bigger on right side. Uterus small and hard.	General peritoneal carcinomatosis and big growth in pyloric region. Bilateral ovariectomy. Uterus retroverted. Small growths on bladder and rectal walls. Very few adhesions.	Right—6½ × 5 × 4 inches. Left—5½ × 4 × 3 inches. Partly cystic and partly solid. Cystic spaces gelatinous.	Typical picture of Krukenberg tumour with copious mucous accumulation and degeneration (figure 4). Wound healed; pain diminished and general condition improved, but she died a month later from anaemia.

a total of 118 cases with Hundley's statistics. In many cases, the diagnosis is missed either due to the primary lesion in the gastro-intestinal canal being too small to be detected, or to the 'occupation bias' of the surgeon or gynaecologist, as Bland Sutton calls it, or to the too late exploration of the abdomen when the secondary growths are far advanced. I had an opportunity of following up 7 cases and operating on 4 of them. A short summary of the cases is given in the table.

The tumour is found in young and old patients as first described by Krukenberg. One has been reported in a girl of 15 and another by Krueger in a girl of 19. The youngest of Krukenberg's series was aged 25. The ages of our patients varied from 26 to 51 years with an average of 39 years. From the case histories, it seems however more common after or at the end of the child-bearing period, though 80 per cent of cases are said to occur before the menopause. It occurs both in multipara and nullipara but more frequently in the latter. Cases in unmarried women are rare; one has been cited by Jarcho (1927).

The case histories suggest that the tumour is not of slow growth as explained by Krukenberg. The longest duration was 12 months in the last case but 3 months only in the fourth. One of Jarcho's cases gave a history of abdominal swelling of only 6 weeks' duration.

There was ascites in all the cases except the last one, blood-stained in 2 of them. In case 3, there was torsion of the pedicle. Novak and Gray (1938) noted free fluid in 4 out of their 21 recorded cases.

The tumour is generally bilateral as described by Krukenberg. Major (1918) quotes the percentage figure as 90. But Bell (1934) says that it is not always bilateral like most metastatic growths of the ovary. Cases 2 and 3 of this series illustrate unilateral involvement.

The macroscopical appearance shows in all cases the uniform enlargement of the ovaries and preservation of the ovarian shape (plate VIII, figure 2). They are of moderate size and generally lobulated. The cut surface shows in every case the general solid appearance with cystic degeneration, while areas of gelatinous appearance are common as seen in the last case.

Krukenberg tumours are generally enclosed in a smooth and firm capsule, seldom showing any surface growth, but cases 1 and 4

showed definite evidence of surface involvement. Except case 5 in which the tumour in one ovary only had to be removed, none of the recorded cases, though some were quite advanced eliciting general peritoneal carcinomatosis, had much adhesions.

The nature of the cells of a Krukenberg tumour has also given rise to much discussion.

Krukenberg in 1896, when he first described the tumour, considered it essentially a sarcoma finding the marked stromal reaction, but noting the presence of groups of large swollen cells with mucoid protoplasm resembling carcinoma cells, he called the tumour a 'sarcoma ovarii mucocellulare carcinomatodes'. Subsequent investigators (Schlagenhauser in 1902, Amann, Cohn, Ewing, Bland Sutton, Major, etc.) have definitely demonstrated that the growth is of epithelial origin and is often secondary to carcinoma elsewhere, especially in the gastro-intestinal tract. Certain observers have also diagnosed the condition as an 'endothelioma of the ovary' (Bode, Fleischmann, Polano, etc.), and Krukenberg himself also described the tumour as closely resembling an 'endothelioma'. There is no case in our series where we suspected the sarcoma-like nature of the growth.

The pathological findings of the cases demonstrate that the epithelial elements may be found in groups of well-demarcated acini or they may be completely or partially broken down, but they invariably show the different degrees or stages of mucoid epithelial change. The accumulated mucoid secretion flattens out the nucleus and pushes it against the cell wall. This explains the usual occurrence of a large number of 'signet cells' in the tumour. In plate VIII, figure 1 (case 5) less degeneration is observed and there are areas showing the characteristics of a typical adenocarcinoma, whereas, plate VIII, figure 4 (case 7) shows the complete breaking down process but both show the particular stromal reaction and 'signet-ring' appearance of the cellular element. It has been shown by various observers, as also seen in some of our cases, that the primary malignant growth in the gastro-intestinal tract need not necessarily be of the mucoid form but it may be of the type of a cirrhus carcinoma or of a linitis plastica.

With the cases in our series, it is not possible to elucidate the method of propagation of this tumour, as no autopsy could be performed on the patients who died, and moreover the ovarian growths were far too advanced with extensive involvement of the stomach, intestines, omentum and general peritoneum. There was involvement of the surface layer of the ovary in two of our cases. Bucher, Kraus, Schlagenhauser and Major explained such involvement by assuming that the cancer cells of the original growth after invading the serosa, were conveyed to the ovarian surface by the peritoneal current and were implanted there

especially at the sites of ovulation. But in the rest of our cases, though the growth was far advanced, the surface of the ovary was free from any extension of growth. Moreover, its selective implantation only on the ovarian surface does not support this theory.

Jarcho could not detect any surface involvement of the ovary in two of his cases with extensive 'peritoneal' carcinomatosis', and supports the more accepted theory of the propagation of the tumour through the lymphatics as originally described by Krukenberg. According to Kehrer, Amann and Jarcho, there is an extensive retrograde lymphatic communication between the stomach and the ovary via the retroperitoneal and then the adjoining lumbar glands as proved by dissection of these glands.

In at least three of our cases the lymphatic glands behind the stomach and around the pylorus were found enlarged and apparently affected.

These cases also do not support the theory of the propagation of the cancer cells in the blood stream as advanced by Ribbert and Kauffman, as no other organ except the gastro-intestinal tract and sometimes the bladder or rectal wall seemed to be involved. None of the cases of the series, even case 5 in which the right ovarian tumour was adherent to the surrounding organs, suggests the direct extension of the growth to the ovary via the adhesions formed with the gastro-intestinal tract.

The bone of contention in the genesis of the Krukenberg tumour lies in whether the growth is primary in the ovary or secondary to carcinoma of other abdominal organs.

Krukenberg regarded the ovarian tumour as a primary growth. But later it has been shown that it is in the vast majority of cases secondary to carcinoma of the stomach, intestinal tract or bile ducts (Kraus, Wagner, Schlagenhauser, Stander, Glockner, Bland Sutton, Jarcho, etc.). Of the 5 cases originally described by Krukenberg, one complained of stomach trouble and one showed carcinoma of the stomach accompanying the ovarian tumour. Ewing (1934) thinks that real Krukenberg tumours are always secondary. Bell (1934) classifies it under ovarian neoplasms—metastasis secondary to gastro-intestinal carcinoma. Graves (1928) called it in the last edition of his book 'Alien Tumours'—metastatic from intestinal tract.

But there are a few cases on record, where all the investigations carried out failed to show any carcinomatous change in the gastro-intestinal tract. During the time of operation no growth was detected anywhere else. The later follow-up failed to reveal any sign or symptom of a growth in any portion of the

gastro-intestinal tract. These are the cases recorded by Krukenberg, Sternberg, Schenk, Glockner, Frankl, Neuman and Andrews. In 1918, Major on reviewing the literature, collected 55 undoubted cases of Krukenberg tumour plus 8 probable cases and of these 63, 16 cases were probably primary in the ovary. Only after a very thorough and careful autopsy one should call a Krukenberg tumour primary in the ovary provided it presents all the macro- and microscopical characteristics. But Novak and Gray (1938) state, citing the cases of Dr. Andrews, Frankl and Neuman, that tumours should be also considered primarily in the ovary if the clinical tests either during the operation or later be negative and if the person lives free from any symptoms of gastro-intestinal cancer for a sufficient number of years after the removal of the ovarian growth. The second case in our series seems to belong to this group where the patient lived for at least 5 years after the operation. All other 6 recorded cases were secondary to carcinoma of the gastro-intestinal tract. Novak explains that the primary growth in the ovary as described by Krukenberg may be of a teratomatous nature where the mucoid endodermic epithelium may be the starting point of the malignant tumour of a mucocellular type. It will be of interest to note that in case 3 the same growth in different areas showed both the characters of typical Krukenberg tumour and also that of pseudomucinous cyst-adenoma.

It is of practical importance with regard to treatment to find out first whether Krukenberg tumour is primary or secondary. During operation on ovarian cancers, the other abdominal organs should be carefully examined and while operating for malignancy of the gastro-intestinal tract the ovaries should be thoroughly investigated. Secondly the extent of involvement of the uterus, tubes and pelvic organs in a case of Krukenberg tumour. In cases 3, 4, 5 and 7, the bladder and uterus seemed involved, while the tubes were affected in 2 cases (1 and 4). Frankl in ovarian carcinoma accompanying primary growth in the gastro-intestinal tract and Jarcho in his 7 cases found microscopic metastasis in the uterus, tubes and vagina. Where the uterus was affected the bladder was also found involved, as in our cases. Again Frankl found the uterus and tubes free from any metastasis in 36 cases of primary ovarian carcinoma. It is agreed that the greatest growth occurs in the ovary accompanying carcinoma of the gastro-intestinal tract. This is explained by some as due to the rich blood or lymph supply or to some hormonal influence. In the case quoted by Major there was an enlargement, increased weight and signs of hyperactivity of the pituitary gland.

The treatment depends on whether the uterus and its appendages are affected or not along with the growth in the ovary, and also how far the metastasis has advanced in the abdominal organs and in the pelvis. According to Schauta, Neuman, Frankenthal, Schlagenhauser and Frankl, the uterus and adnexa should be removed. Some of them go so far as to perform partial gastrectomy in early cases of involvement of the stomach. Jarcho (1927) says that 'it is hardly justifiable to remove carcinomatous organs while other organs also are affected.' According to Shaw (1932) and Jarcho (1927) 'there has been a failure of both surgery and x-rays and time has yet to show the ideal treatment.'

It has been noted by all observers, that no case of Krukenberg tumour of the secondary type is cured by operation. Our records support this view. They die soon after from further gastric trouble. But we have noted, especially in cases 5 and 6, that the symptoms of pain, restlessness and general weakness are all relieved after the operation. Thirteen patients out of 21 cases recorded by Novak died within 6 weeks to 14 months after the operation, and in 3 others death was obviously imminent. The result of operation in a Krukenberg tumour of the primary type seems to be quite favourable, as seen in our case 2 and also in those cited by Andrews, Frankl and Neuman.

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PSEUDO-PARALYSIS DUE TO SCORBUTIC EPIPHYSITIS

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THE term 'scurvy' brings to one's mind a picture of bleeding gums or purpuric patches on the skin. It is not sufficiently recognized that a state of pronounced vitamin C deficiency may occur without either of these manifestations.

A clinical condition very frequently met with in Gujerat is a 'pseudo-paralysis' of the legs due to scorbutic epiphysitis. The term pseudo-paralysis is used because in nearly every case the diagnosis of paralysis has already been made by the practitioner or parent.

The previous history is usually that the child has suffered from some infectious disease or debilitating malady such as typhoid, measles, dysentery or smallpox. After convalescence it is found that the child refuses to walk or even stand. The child is fretful, crying, loses weight and declines to eat. There may be slight fever.

In typical cases, the attitude of the child is characteristic and almost pathognomonic, and bearing the condition in mind, one may 'spot' the diagnosis as soon as the parent presents the child for examination. Held up by the arm-pits, the child keeps its thighs and legs flexed up in mid-air. If an attempt is made to place the child on its feet, it refuses to bear its weight on its legs and withdraws its feet and flexes its legs more. If the legs are straightened, the child cries with pain. The legs are obviously not paralysed, but as the child refuses to walk or even stand, the impression of paralysis is often incorrectly gained by parents and even doctors. Frequently cases are seen, which have been treated as paralysis, rheumatism, tuberculosis or osteomyelitis for weeks or even months on end. The doctors have prescribed every vitamin except vitamin C, with the result that the child has drifted into chronic invalidism and the parents into disconsolate despair.

On being questioned, the parents invariably and emphatically reply that the child never eats fruits. In most cases, the child seems to have an aversion to fruit and has always obstinately refused to eat any.

One week's treatment with vitamin C has the miraculous effect of converting an apparently

hopelessly paralysed child into a practically normal child, able to stand and walk.

The gums are usually normal. In some cases, however, the usual scorbutic changes are seen in the gums, but the striking point is that they are more frequently normal than otherwise. In only 7 cases out of 30 were there scorbutic changes in the gums. The fact that an obvious case of vitamin C deficiency can show epiphysitis and not scorbutic gums is no more remarkable than that an advanced case of rickets can occur with all the usual skeletal deformities and yet have normally developed teeth.

Purpuric hæmorrhages in the skin were not seen in any case of this series. In adults, cases of scorbutic purpura are frequently met with, but none have been encountered in this series of children's cases of pseudo-paralysis. The skin is not hot nor changed in colour, and shows no inflammatory changes.

The knees are the joints usually affected. They present a diffuse, rounded swollen appearance, tender to palpation and painful on passive movement, especially extension.

Not infrequently, however, in cases presenting the characteristic flexed attitude of the knees and with the usual history of deficient intake of vitamin C, the knees appear externally quite normal. A skiagram will, even in such cases, reveal that there is scorbutic epiphysitis (*vide infra*).

Occasionally only one knee joint is affected. The diagnosis is then more obscure. I have seen cases in which only the hip joints have been affected. I have seen no case in which the upper extremity was affected.

Subperiosteal scorbutic hæmorrhages may occur. In one case, an extensive extravasation of blood under the periosteum of the femur, in a bottle-fed baby of 11 months, led to an incorrect diagnosis of osteomyelitis. In one week with appropriate therapy, the swelling had dramatically subsided. Such an extravasation of blood may occur over the spine, in which case a diagnosis of tuberculosis of the spine may excusably be arrived at.

Three classes of cases may thus be described:—

(1) Epiphysitis with swollen joints, usually the knees.

(2) Epiphysitis complicated with subperiosteal extravasation of blood. Such cases

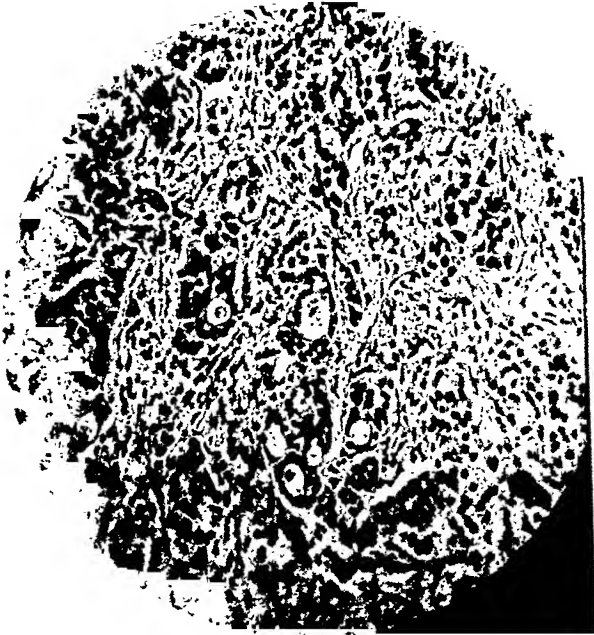


Fig. 1. High power.—Areas showing well-demarcated acini as in adeno-carcinoma but with stromal reaction and 'signet-ring' cells present.



Fig. 2.—Bilateral tumours along with uterus containing a fibromyoma—irregular; hard and indented.

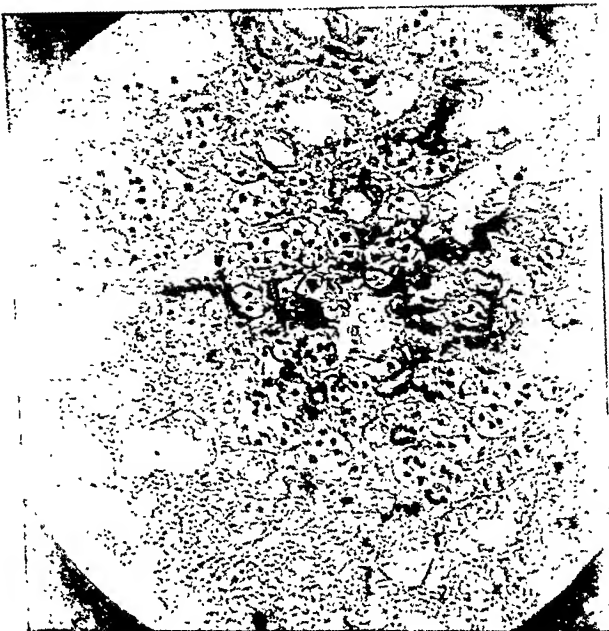


Fig. 3.—Typical group of 'signet-ring' cells.



Fig. 4.—Showing an advanced stage of degeneration and with copious mucous accumulation in cells.



Fig. 1.



Fig. 2.



Fig. 3.

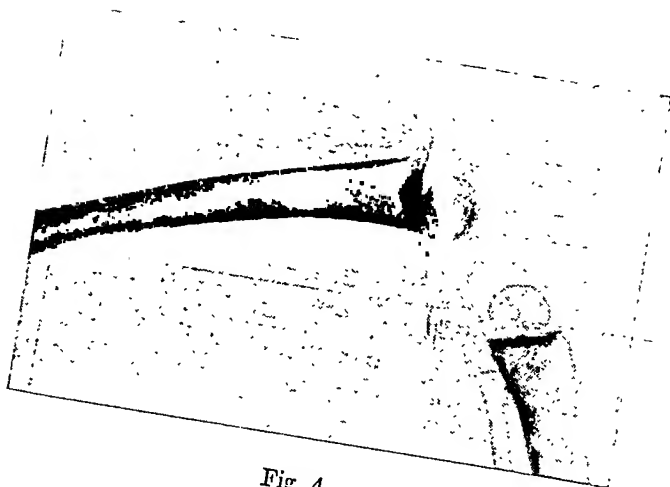


Fig. 4.

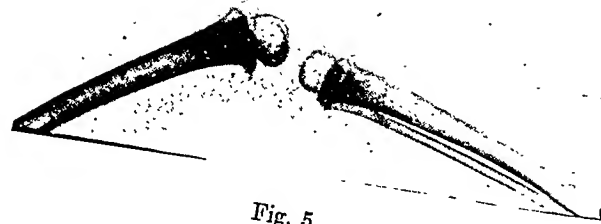


Fig. 5.

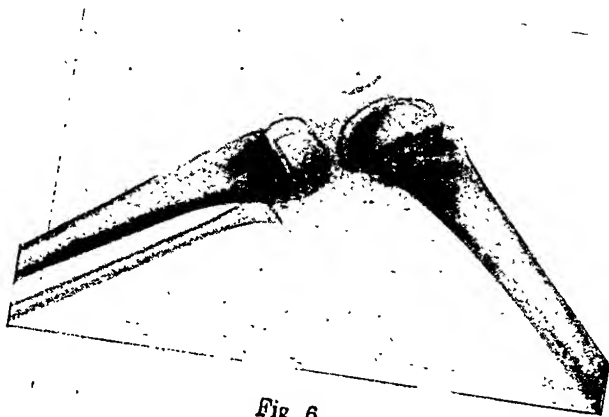


Fig. 6.



Fig. 7.

present a considerable swelling and simulate acute osteomyelitis.

(3) Cases with normal appearance of knee joints. The parents complain that the child is always stumbling and falling and is unsteady on his feet. At times the child may even 'go off his feet' and refuse to walk at all. There is no pain in the knees and no swelling. A skiagram will, however, show the changes described below.

Diagnosis

(1) The characteristic attitude of the child can be considered of diagnostic value.

(2) Other signs of scurvy, e.g. purpuric spots, bleeding gums, may be looked for.

(3) The skiagram is diagnostic. A dense irregular band, obviously containing an excessive amount of calcium, is seen at the end of the diaphysis. This is the provisional bone laid down by the epiphysis, and it is composed of unorganized calcium phosphate. This appearance is diagnostic of scorbutic epiphysitis. This provisional bone is friable and often breaks, and there may be hæmorrhages in this area and microscopic fractures or dislocations of the epiphysis. The neighbouring zone is greatly decreased in density so that the bone may not be visible. The essential disturbance seems to be failure of the osteoblasts to convert provisional into true bone. The true bone of the shaft is rarefied, in striking contrast to the provisional bone. The shaft looks blurred—the so-called ground-glass appearance.

Plate IX illustrates these three features.

(4) Failure of the urine to decolorize dichloro-phenol-endo-phenol after administration of ascorbic acid. In one child three tablets of ascorbic acid 50 mg. each and one injection of 'Redoxon' 50 mg. were given. The urine subsequently passed did not decolorize dichloro-phenol-endo-phenol, indicating a marked deficiency of ascorbic acid.

(5) Improvement on vitamin C therapy, given orally and parenterally, will confirm the diagnosis.

Differential diagnosis

(1) *Infantile paralysis*.—Many cases are referred with this diagnosis and have had prolonged therapy with vitamin B, to no advantage. On careful scrutiny, it is obvious that the legs are not paralysed.

(2) *Tuberculosis*.—The slightly expanded knee joint may suggest tuberculosis, but the bilateral nature of the condition should cause further reflection.

(3) *Acute rheumatism*.—In scorbutic epiphysitis, the condition remains limited to the knee joints, whereas in acute rheumatism the condition flits from joint to joint.

(4) *Acute osteomyelitis*.—If there is an extensive subperiosteal extravasation of blood, acute osteomyelitis may be thought of, but the leucocyte count will not be raised and the child's condition will not be so critical as in acute osteomyelitis.

(5) *Rickets*.—In rickets, the bone ends are expanded at the joints, and the skiagram shows a cup-shaped epiphyseal cartilage, quite distinctive from the radiological appearances in scurvy.

The doctors' note, attached to one case, is given below in full, as it illustrates the common fallacies in diagnosis and treatment.

'The patient has been under the treatment of various doctors since the last 4 months for daily rise of temperature and pain in the lower extremities. Two months back he was referred to me for continuous fever. He had at that time enteric fever complicated with jaundice which condition cleared up in due course. In the meantime, my attention was drawn to the localized swelling in the lumbo-sacral region which was tender and bearing relation to the pain in the lower extremities. The relatives are convinced that the spine is affected and the patient is sent for radiogram. He is having Adol drops and Osteo-calcium tablets and a mixture containing calcium, iron and bitter tonic. He is advised plaster of paris jacket.'

As the child was presented to me by the parents, the diagnosis was obvious. Both knees were flexed acutely in the mid-air and the child screamed as I tried to straighten the legs. The lumbo-sacral swelling was a scorbutic hæmorrhage tender to touch. The gums were bleeding. This point had been overlooked by the doctor. When I questioned the parents as to the child's diet, they admitted that the child obstinately refused to take any fruit at all. The white cell count was normal.

Treatment

Ascorbic acid is given in large doses, orally and parenterally.

Local treatment is unnecessary, but frequently lead lotion, belladonna and glycerine are prescribed as placebos.

As auxiliary treatment, cod-liver oil and ultra-violet light are given.

Fruit is insisted on as a part of the diet.

Prognosis.—With the correct diagnosis in mind, it is most gratifying to be able to reassure the parents and predict that, with the

proper treatment, the child will be showing distinct improvement within a week.

Cases relapse if correct diet is not given subsequently. Some cases relapse each year.

TABLE
Summary of cases

Number	Sex	Age in years	Caste	Parts affected	Duration	Precipitating factors
1	F.	4	Bania	Legs, gums	2 years	
2	M.	2½	Jain	Legs	20 days	Smallpox.
3	M.	4	Patel		1 month	Measles.
*4	M.	½	Mohammedan	Ankles	1 "	Rickets.
5	F.	1½	Christian	Legs	15 days	
6	M.	½	Patel	Knees	2 "	Diarrhœa.
7	M.	6	Bania	"	4 months	
8	M.	1	"	"	"	Cirrhosis liver.
9	M.	3	Patel	"	10 days	
10	M.	3	Bania	"	1 month	
*11	M.	2	Patel	"	8 days	
*12	M.	3	Christian	"	"	
13	M.	4	Hindu	"	2 months	
*14	M.	7	Bhavsar	Right leg	15 days	
15	M.	4	Brahmin	Knees	4 months	Enteric fever.
16	M.	2	Dhed	Knees, gums	10 days	Fever.
*17	M.	5	Bania	Right hip	25 "	Dysentery.
18	M.	10	"	Knees	"	
*19	F.	4	Darji	"	2 months	A fall.
20	M.	4	"	"	2 "	Diarrhœa.
*21	M.	3	Bania	Spine, gums	"	A fall.
22	F.	6	Christian	Knees	2½ months	Diarrhœa.
23	F.	2	Bania	"	3 "	
*24	M.	11/12	Mohammedan	Knees and femur	"	Malaria.
25	M.	4	Bania	Knees	"	Pneumonia.
*26	M.	5	Soni	"	2 years	
*27	F.	7	Bania	Knees, gums	2 months	Malaria.
28	F.	4	"	" "	"	Rickets.
*29	M.	9	Bania	" "	1 year	Tonsils.
30	F.	2	"	" "	"	

Further notes on the above cases

No. 4. Recovered under treatment. Recurrence 6 months later. Re-admitted.

No. 11. Recovered in 4 days.

No. 12. Three attacks.

(1) Both knees, one year ago. Recovered.

(2) Recurrence—discharged, walking in one week's time.

(3) Recurrence after one week—unable to stand—recovered in 24 hours with large doses of vitamin C.

No. 14. A similar attack one year previously—recovered with fruit. No fruit given since—hence recurrence.

No. 17. Simulating infantile paralysis—recovered in 15 days.

No. 19. Treated for two months as 'pus' and given vitamin D. Improved in a week.

No. 21. Spine very tender—diagnosed as T. B. spine. Recovered in a week with vitamin C.

No. 24. Subperiosteal hæmorrhage left femur simulating acute osteomyelitis—a bottle-fed baby—gums normal. In one week, swelling subsided with vitamin C.

No. 26. Does not walk properly at times. Frequently stops walking.

No. 27. Attacks recur yearly in September and October.

No. 29. Pain and stiffness in both knees once every year. Bleeding gums.

CORRIGENDUM

In the March 1945 issue of the *Indian Medical Gazette*, on page 133, column 2, line 22, the number '252' should be '2052'.

EXPLANATION OF PLATE IX

Fig. 1.—Showing the characteristic posture when held supported by the axillæ.

Fig. 2.—Showing the characteristic posture which may be considered a diagnostic sign.

Fig. 3.—Same child, as in figure 2, now able to stand after one week's treatment with vitamin C.

Fig. 4.—Skiagram of child, aged 11 months, artificially fed, never given fruit.

(a) Extensive subperiosteal hæmorrhage.

(b) Dense, irregularly formed, provisional bone.

(c) Microscopic dislocation of epiphysis.

(d) Zone of diminished density.

Complete recovery with vitamin C therapy.

Fig. 5.—Skiagram of child, 4 years age, knees swollen and tender.

(a) Dense provisional bone of epiphysis.

(b) Microscopic subluxation.

(c) Zone of diminished density.

Unable to walk 2 months. Improved in one week on vitamin C treatment.

Fig. 6.—Skiagram of child, 7 years age. Unable to walk 2 months. Knees held in typical posture but no obvious swelling. Pain on pressure and extension. Gums and teeth hypertrophic and bleeding slightly. History of relapses annually in September and October.

(a) Extremely dense and irregular provisional bone of epiphysis.

Fig. 7.—Skiagram of child, 2 years age. Knees not swollen but pain on extension. Typical posture. Bleeding gums; never eats fruit.

(a) Irregular provisional bone.

(b) Zone of diminished density.

A Mirror of Hospital Practice

OVARIAN TUMOUR IN A THREE-YEAR-OLD CHILD

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THIS child was admitted to hospital on 24th August, 1944, with the history of a swelling moving about in the abdomen, noticed by the mother 8 days before.

On examination, the areolæ in the breasts were pigmented, large and firm, and the vulva more fully developed than usual. A large freely movable hard lump in the lower half of the abdomen was felt rising out of the pelvis and reaching above the umbilicus; it was not painful or tender. On rectal examination the lump was felt in close relation to the left side of the uterus but not attached to it. The uterus was large, for the age of the child.

The red cell count was 4 millions; hæmoglobin 65 per cent. The urine showed a trace of albumin; stools nothing abnormal.

A diagnosis of left ovarian tumour was made. The child was kept in bed, on full diet and plenty of fruit juice and glucose. Six days later, the abdomen was opened under general anæsthesia and a large left ovarian tumour was removed. The right ovary was normal. There were no adhesions to the adjacent organs.

The tumour was roughly spherical, solid and about 4½ inches in diameter; on section the capsule was thick, the tumour being yellow in colour and uniform in appearance. The District Laboratory reported that it was a granulosa cell tumour and Professor Bhaskara Menon of the Vizagapatam Medical College stated: 'It is a lutenizing granulosa cell tumour. It is of interest as it shows in places superficial resemblance to hypernephroma'.

Shortly after the operation the child started a temperature up to 103°F. which came down to 101°F. next day. Blood films showed no malaria parasites. There was vaginal bleeding which lasted for two days. The breasts were full and began to secrete milk from the third day after operation. The urine gave positive Aschheim-Zondek test.

The wound healed in a week. The secretion of milk stopped but the size of the breasts showed no change. The child was discharged a month after admission.

I am grateful to my chief, Colonel L. K. Ledger, I.M.S., for permitting me to record this case and to Major Manifold and Prof. T. Bhaskara Menon, for their valuable reports.

PERSISTENT INTRACTABLE HEADACHE IN AN ADULT CAUSED BY *ASCARIS LUMBRICOIDES*

By P. K. GHOSH, M.B.

ASCARIDIASIS shows no predilection for any sex or age, but the graver symptoms are usually encountered only in the young. From minor intestinal disorders to serious abdominal complications, e.g. intestinal obstruction, appendicitis, liver abscess, even perforation of the gut, all have found mention in textbooks. Ascariasis is known to produce complications in other organs as well, e.g. broncho-pneumonia (Low); even meningismus is recorded (Horder). But all these complications are met with in children. Adults do commonly suffer from ascariasis in the tropics but they seldom manifest data adequate for a correct diagnosis.

The following case illustrates how a persistent intractable headache in an adult was traced to *Ascaris lumbricoides* alone.

A Hindu male, aged over 50, had been treated at civil hospitals at different times for the only complaint of a persistent intractable headache of 'boring' nature. He had been subjected to various examinations in hospitals, but nothing definite could be detected, except errors of refraction for which suitable glasses were prescribed but without effect. Analgesics could only afford him a transient relief.

To start with he was put on antineuralgic drugs with calomel. The calomel given for a few days set up mercurial stomatitis, and it was replaced by magnesium sulphate. Soon after this the patient vomited two big round worms. Anthelmintics were therefore given and seven more round worms were passed with evacuations, and his long-standing headache came to an end. Thereafter no headache was complained of.

A CASE OF POST-INFLUENZAL GRANULOCYTOPENIA TREATED WITH LIVER

By K. C. CHAKRAVARTY, L.M.F., L.T.M.

A TEA garden labourer, aged 44, was admitted to the hospital on the afternoon of 21st June, 1944, suffering from fever. He stated that that morning the temperature rose abruptly with rigor and chill. His other complaints were

intense headache, sneezing and nasal catarrh, vague pain in the abdomen and pain all over the body, and constipation for two days. On examination, temperature 103°F., pulse 122, respiration rate 23, lungs clear, heart normal, liver not palpable, spleen enlarged two fingers, abdomen tender, tongue slightly coated. The peripheral blood did not show any malaria parasite. The differential count was: polymorphs 65 per cent, small lymphocytes 20 per cent, large lymphocytes 9 per cent, transitional 5 per cent and eosinophile 1 per cent. The case was clinically diagnosed as influenza.

A soap and water enema was given after admission followed next morning by a purgative. A diaphoretic mixture and the usual influenza mixture (containing sodium salicylate) were prescribed twice daily alternately. The temperature came down to normal and the patient was feeling better except for debility.

On the seventh day of the illness, however, the patient was somewhat listless and prostrated and complained of nausea, disinclination for food, severe pain in the loins and legs, soreness of mouth and tongue. Next day the condition became more acute with hiccough and pain in the abdomen, frequent vomiting and violent diarrhoea, about 15 motions being passed during the day. Microscopically nothing pathogenic was found in the stool. The pulse rate was 125 and the temperature 96.2°F. The peripheral blood was taken for a differential count but only a few granular cells could be detected. Venous blood showed: total r.b.c. 4.2 million per c.mm., total w.b.c. 900 per c.mm. In differential count neutrophils were 9 per cent and the rest lymphocytes and monocytes. These findings with the clinical condition suggested a diagnosis of 'acute granulocytopenia'. As 'pentnucleotide' or liver extract was not available, 2 c.cm. of milk was given intramuscularly. The condition became worse next day with extreme toxæmia and prostration; temperature 95.4°F., pulse 168; mild delirium and restlessness were present. Rectal saline with glucose 10 per cent was given with other symptomatic treatment. Four ampoules of hepolon (Allen & Hanbury's) were procured and was given for four days, one ampoule per day. The diarrhoea ceased and after the fourth injection the symptoms abated considerably. Regeneration of neutrophils was evident in the blood picture. The

patient continued to maintain progress both clinically and hæmatologically and was discharged three weeks after admission.

Discussion.—Acute agranulocytosis, according to modern literature, is not an infrequent complication after administration of sulphonamides and pyrimidon; it has also been observed and recorded descriptively in certain cases of kala-azar and/or following intravenous injection of pentavalent antimonials by workers in China, Zia and Forkner, and Huang. The first authentic case of kala-azar recorded in India with this complication has been discussed by Das Gupta and Sen Gupta. In the post-influenzal phase of the vast majority of cases this complication is absent and no case of granulocytopenia following influenza has been recorded before in this country.

The mechanism which leads to neutropenic changes in the bone marrow by arresting maturation of myeloblasts is still not clear, though some workers stress the point that this syndrome can be produced by any toxic or infective agent. It appears to the writer that some toxic substance produced in the blood during the course of certain diseases and/or following the administration of drugs, notably the sulphonamide group, may cause dissolution of granulocytes in the systemic circulation or retard formation or maturation of young myeloblasts.

Summary

1. The clinical picture of a case of post-influenzal granulocytopenia is described.
2. The diagnosis was confirmed by the scarcity of granular cells in the peripheral blood film.
3. In the absence of pentnucleotide, small doses of liver injections effected a cure in the case.
4. It is suggested that the susceptibility of individual granular cells in the systemic circulation or in their young stages in the bone marrow to some toxic substance produced in the blood during disease and/or following administration of drugs may chiefly be responsible for the production of neutropenic changes as evidenced by the extreme paucity of granular cells.

Acknowledgment.—I am thankful to Dr. G. G. King, Medical Officer, Mangaldai Medical Association, for kindly permitting me to publish this case report.

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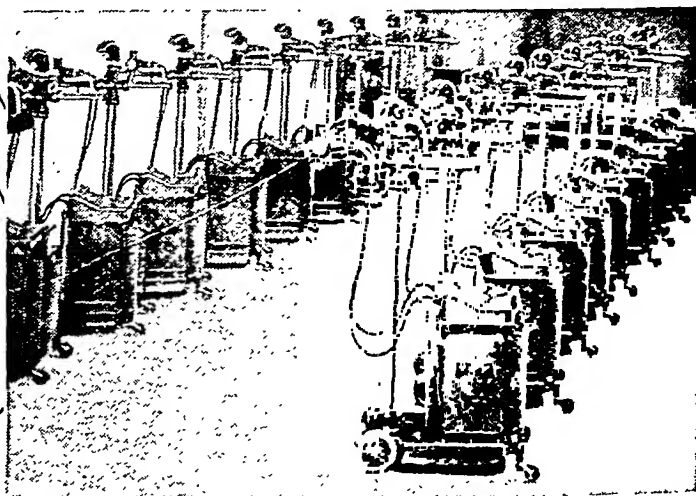
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Indian Medical Gazette

MAY

THE COPPER-SULPHATE SPECIFIC-GRAVITY METHOD OF BLOOD ANALYSIS

IN the tropics in general and in India in particular, cases of hypoproteinæmia and of anæmia are common. The physician often wants to know what are the blood hæmoglobin and protein values of his patients. The hæmoglobin value in grammes can be obtained rapidly by the hæmoglobinometer if the physician has one, but hæmoglobinometers are difficult to procure in these days; the figures for total blood proteins can be obtained only by a long and tedious biochemical examination. It therefore appears to be of considerable interest and importance to the medical profession in India that a simple method has been published which gives approximate figures for total blood proteins and for hæmoglobin.

The method consists of finding out the specific gravity of (a) whole blood and (b) plasma by letting drops fall into a series of bottles containing copper sulphate solution of varying specific-gravities. Simple methods of making up these solutions without a specific-gravity bottle or even a chemical balance are described. The editor has carried out careful tests of this method of analysis of blood and the results of these tests will be published later. At present, it should suffice to say that when carefully carried out the results of the test appear to be sufficiently accurate to be of great value to the clinician; their value to the research worker requiring a greater degree of accuracy is less, but may still be considerable.

Briefly the findings of the tests carried out by the editor are as follows:

In 40 bloods selected as showing a wide range of hæmoglobin values varying from 4 grammes to 16 grammes it has been found that the hæmoglobin value as given by the copper sulphate specific-gravity method has usually agreed quite closely with that given by a careful estimation

with Hellige hæmoglobinometer. Out of 40 cases in only 6 has the difference in values been more than 1 gramme; in 19 cases the difference has been less than $\frac{1}{2}$ gramme and in the remaining 15 it has been between $\frac{1}{2}$ and 1 gramme. These facts indicate that as a rough method of hæmoglobin estimation the test has considerable value. Since however the test with the ordinary hæmoglobinometer is simple, rapid and accurate, provided that the hæmoglobinometer can be relied upon, the hæmoglobinometer will usually be preferred where it is available. One army medical officer however has told the writer that he has used this copper sulphate specific-gravity method as a method of testing doubtful hæmoglobinometers!

While the figures given by this for the hæmoglobin have been reasonably accurate, the figures given for the hæmatocrit readings in our cases have been persistently too low. This fact would suggest that the method given for calculating the hæmatocrit reading has been defective, and this defect may be removed; but even then our findings suggest that the test will be of limited value in this particular respect.

For clinicians who have reliable hæmoglobinometers, the main value of the test will be that it gives one the total blood protein values with considerable accuracy. A parallel series of estimations carried out by the editor by the copper sulphate method and by Dr. J. P. Bose by the long and laborious method of Kjeldahl has shown the copper sulphate method to be accurate enough for all clinical purposes, giving the total blood protein within $\frac{1}{2}$ gramme and usually within a narrower margin than this. The limitation of the copper sulphate method is, of course, that it does not give the albumin-globulin ratio which is often important to clinicians. Nevertheless the test should be an extremely useful one. One great advantage of this test is its rapidity and simplicity, the result being available in a few minutes instead of many hours, possibly one or two days later. We recommend this test very strongly to our readers. The details of the test are given in the 'current topics' section of this issue; also the line chart necessary for calculating the plasma proteins and hæmoglobin values is reproduced in this issue. An article giving our experience of this test will appear in a future issue of this journal.

J. L.

AGRANULOCYTOSIS

LEUCOPENIA with a diminution in the number of neutrophils is fairly common in certain diseases prevalent in this country, *viz*, kala-azar, chronic malaria, the dengue group of fevers, and typhoid, but these are not usually associated with any obvious recognizable signs directly attributable to the blood changes; the one exception is in kala-azar with the occurrence of cancrum oris and other complications. In the clinical entity known as agranulocytosis, the leucopenia is much more marked than in these conditions; the white cell count may drop below a thousand per cubic millimetre with few or no granulocytes but without any significant decrease of the red cells and hæmoglobin; there are associated fever and necrotic ulcerations in the mouth and throat.

This condition has come to the fore in recent years as a complication encountered in connection with the use of certain common drugs, although it occasionally occurs in some infections such as severe forms of pneumonia, septicæmia, etc. Following the clinical discovery of the condition by Schultz in 1922, its recorded incidence rose high till 1933, when the causative rôle of amidopyrine was discovered. Thereafter, as a result of restrictions on the sale of this drug, it seemed to decline. Since the advent of the sulphonamide group of drugs, cases of granulocytopenia or of actual agranulocytosis have become more frequent again. Other drugs such as benzol, barbiturates, gold salts, organic arsenicals, etc., have also been known to give rise to this condition, and the latest is thiourea which is used in the treatment of hyperthyroidism.

To what extent the condition is caused by these drugs is not known. All that we know is that there was a noticeable increase in its incidence with the increase in the use of sedatives of the amidopyrine group, especially those containing amidopyrine with a barbiturate. It is one of the rarer complications of sulphonamide therapy; nevertheless precautions are taken to check the white cell count at regular intervals in any patient on sulphonamides for more than a week.

Since the introduction of arsenical preparations in the treatment of syphilis, toxic effects on the hæmopoietic system have been reported, but in view of their widespread use, the occurrence of agranulocytosis following their admin-

istration must be regarded as a rare complication. According to a recent report, there were only 24 'blood dyscrasias' in a series of 1,244,537 injections given in the United States Navy between 1925 and 1938. We are not aware of reports of this kind in this country, but for the present we may refer our readers to a case of tropical eosinophilia, published in the March issue, developing agranulocytic angina during arsenical therapy. The patient showed signs of intolerance to acetylarsan by febrile reactions after the third and fourth injections, and her condition became acute after the fifth injection. The reason for the development of agranulocytosis after administration of arsphenamines has been a matter of much speculation. It has been suggested that the benzene ring in the arsphenamine molecule, and not the arsenic itself, is the factor concerned in the production of these toxic effects. The harmful effects of benzol on the bone marrow is well known, and a benzene ring is also present in the sulphonamides and amidopyrine. It is also probable that, in at least some of the cases, the condition is an allergic and not a toxic phenomenon. The fact that it may set in abruptly after relatively small doses, and with treatment rarely lasting less than ten days, lends support to this view. In the case just referred to, the patient developed sensitiveness to the drug ten days after the treatment was begun. According to Witts, as little as 1 to 2 grammes of amidopyrine has been sufficient to sensitize some persons, and once the patient is sensitized, a dose as small as 0.2 gramme may precipitate an acute attack of agranulocytosis; the complication occurred after a total dosage of 18 grammes of sulphonamide and an average daily dose of 2 to 3 grammes in a collected series of 20 cases. On the other hand, many patients have been given much more than this without any untoward effect. These facts point to personal idiosyncrasy as an important factor; when this is the case, the drug, after a preliminary sensitizing dose, may depress the leucoblastic tissue to the extent of inhibiting the production and delivery of the neutrophils.

It is not clear why certain infections are liable, though rarely, to cause agranulocytosis; it may be due to the overwhelming nature of their attacks. There may be some truth in the suggestion that the myeloid tissue varies with

the individual; in persons with 'weak' bone marrow, a moderately severe infection may exert a very baneful effect. So far, we have scarcely associated influenza with this complication, but, as will be seen from a report elsewhere in this issue, such an attack was followed by agranulocytic angina.

In treatment, there is no specific remedy; early diagnosis and withdrawal of the offending drug are of prime importance. Although this alone may suffice to restore the blood picture to normal, especially if the agranulocytosis is not of marked degree, pentnucleotide should be administered without delay. Favourable results have been obtained if it is started early, preferably within four days, and if it is given in adequate doses, *viz*, 10 c.cm. (containing 0.7 gm.) four times a day for at least four consecutive days. The chances of recovery are reduced if the treatment is begun late, as absolute agranulocytosis for seven days is incompatible with life. Pentnucleotide is however of no value if the bone marrow is in an inactive state, producing no leucocytes, as can be judged from sternal puncture; in such cases a blood transfusion may tide over the crisis.

Liver extract has also been recommended as a useful therapeutic agent. Both the patients referred to above had liver, as pentnucleotide

was not available; the authors believe that it was responsible for the cure. Some have also used liver extract as a supportive measure in the treatment with arsenicals or heavy metals of patients with a previous history of intolerance to these drugs. In animal experiments with thiourea, agranulocytosis has been prevented by the simultaneous administration of liver. The value of liver extract injections in these cases probably lies in its beneficial effect on the bone marrow and liver function.

Finally, the question arises whether the sulphonamides, though leading to agranulocytosis, may not be used in treating any dangerous secondary bacterial infection which accompanies it. This line of treatment has recently been adopted in a few cases with encouraging results; the granulocytes which had previously disappeared began to reappear in the blood within a few days, pyrexia disappeared, and the patients made good recoveries. Similarly, granulocytopenia resulting from severe bacterial infection is not in itself a contraindication to sulphonamide therapy, if the causative organisms are susceptible to the drug. But penicillin will probably be the drug of choice in these cases.

R. N. C.

Special Article

INDIVIDUAL VARIATIONS IN THE ABSORPTION OF DRUGS FROM THE GASTRO-INTESTINAL TRACT

By COLONEL SIR R. N. CHOPRA, C.I.E., M.A., M.D.,
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Introduction

FROM the point of view of absorption, the alimentary tract has been divided into three main sections. These sections are not anatomical but purely from considerations of function. The upper portion comprises the mouth, the stomach and the upper part of the duodenum. Its functions are to receive food, to reject unsuitable material, to reduce the re-

mainder to a fairly uniform consistency by chemical and mechanical means. The digestion of food is started here, and the contents are passed on to the middle portion.

The middle portion begins in the lower part of the duodenum and extends to the ileo-cæcal sphincter. Its functions are to complete the digestion of food and to absorb as much as possible. Nearly 90 per cent of the absorbable substances in a meal are taken up here.

The lower portion consists of the cæcum, the colon and the rectum. Its functions are to complete absorption, to store and to periodically excrete the indigestible residue. The contents of the small intestine enter this portion in a fluid state, and are reduced to a semi-solid consistency. Certain reflexes are set up periodically and the contents are expelled.

Absorption from the rectum and colon is small, and their utility from the point of view of nutrition or medication is very limited.

In order to understand individual variations in the absorption of drugs, it is essential to grasp these facts, because absorption of drugs is intimately connected with the digestive processes. It is also worthy of note that the majority of gastro-intestinal troubles are due to the disorders of the upper and the lower portion of the alimentary canal. The stomach has to bear the brunt, in the first instance, of all indiscretions in the matter of diet, and frequently suffers severely from liberties which are taken by an individual with regard to food and drink. The lower portion also suffers frequently from the effects of faulty dietary, but whereas infective conditions do not affect the stomach, on account probably of its strong acid juice, the lower portion is frequently involved in both protozoal and bacterial infections. The middle portion is often the seat of infestations with helminthic parasites, some of which attach themselves to the mucous membrane while others merely live on the nutrient fluid round them.

The main factors concerned in individual variability in the absorption of drugs may be grouped under three headings:—

I. Variations because of physiological factors.—The most ancient, the most natural and even now the most widely used method of administration of drugs is by the oral route. Its chief advantages are undoubtedly from the point of view of the patients who can make use of medicaments without the intervention of the doctor or any other person. A majority of the drugs given by mouth reach the stomach without much alterations on account of rapid passage through the mouth, the pharynx and the œsophagus. No appreciable absorption takes place even from the fundus of the stomach. It may be stated here that in case of some drugs considerable absorption may occur from the mucous membrane of the mouth, and this method is adopted in case of some diffusible drugs (e.g. nitro-glycerine, adrenaline, some sex hormone preparations), but this cannot be regarded as a suitable method for most of the other drugs in use. It is only when a drug passes through the pyloric sphincter that the absorptive processes really begin. The activity of the stomach, therefore, plays an important

part in the commencement of absorption because it is the muscular contractions of this organ, which push the contents through the pyloric sphincter after they have been dealt with by the gastric juice. The passage of a drug through the stomach may thus take from a fraction of a minute to more than two hours.

If a non-irritant drug is swallowed when the stomach is empty, and, when a large quantity of water is taken with it, it rapidly passes through the stomach into the duodenum and absorption commences immediately. If, however, a drug is taken after a meal, its absorption is very variable. For instance, if a non-irritant drug is taken with a large amount of fluid, it may pass along the lesser curvature of the stomach straight to the pylorus and through it into the duodenum. If the volume of fluid is small, the drug will mix with the food mass, pass slowly through the pylorus with the food and absorption will be considerably delayed. Absorption of a drug from an empty stomach is often irregular specially if it is irritant, as it may reflexly cause closure of the sphincter and thus prevent its reaching the absorptive surface of the duodenum.

Circulation of blood in the gastro-intestinal tract has considerable influence on absorption. Absorption is quick when the circulation is normal; it is slowed when it is hampered by such factors as vaso-constriction, catarrhal conditions of the mucous membrane, etc.

It will thus be seen that large individual variations in the absorption of drugs taken by mouth would take place if drugs are given without due regard to the physiological considerations as is not infrequently the case. If the physiological processes regulating the activity of the gastro-intestinal tract are borne in mind, it would be easy to insure either slow or rapid absorption within certain limits. It may be taken as a rough rule that absorption of about three quarters of a dose of a drug should usually occur between one to three hours after its administration by mouth.

II. Variability because of physical and chemical factors concerned.—The second group concerned in the individual variability in absorption of drugs are physical and chemical factors. The phenomena of solution, filtration, osmosis, diffusion, dialysis, and phagocytosis are all actively concerned in the absorption of drugs. In addition to these,

a mechanism which is not understood occasionally comes into play. This has been termed the 'vital activity' of the cells of the mucous membrane, and defies all the physical and chemical laws and endows the cells of the mucous membrane concerned with special powers of selection or rejection of the material at its disposal. Absorption of the animal's own serum, for example, takes place from the intestinal canal without alteration whereas other sera undergo normal protein digestion.

The rate of absorption of a drug is modified by the solvent used. For instance, alcoholic solutions are more rapidly absorbed than aqueous solutions, probably because of the greater diffusibility of the solvent. The more soluble a substance is in the protoplasm the more quickly it is absorbed, *e.g.* glucose, urea, colloidal substances, such as gums, resins, oils, kaolin, etc., are absorbed with difficulty; in fact, when absorbable materials (*e.g.* salts, alkalis, etc.) are mixed with such substances, the rate of their absorption may be so much slowed that no action occurs, the rate of excretion being as rapid as absorption.

The concentration of solutions affects the rate of absorption in conformity with the laws of osmotic pressure. Saline solutions such as magnesium sulphate which are little absorbed themselves may prevent the absorption of readily absorbable drugs. Astringent substances tend to lessen absorption. Solids are not suitably altered by the intestinal juices and are not absorbed except through the phagocytes; they may even then be deposited in the lymphatic tissues. They exert no action unless dissolved by body fluids.

III. Variation in absorption due to disease.

—The third factor concerned in the individual variability in absorption is the disease factor. When the normal functions of the stomach are deranged on account of disease, considerable changes occur in the absorption of drugs. Thus in case of shock absorption is considerably decreased and may even stop altogether. Slight irritation of the gut, which does not cause injury, increases absorption, but absorption is decreased and may be totally inhibited when the gut is injured.

In febrile states, it would not be safe to estimate the probable rate of absorption. In a sick person the rate of absorption may differ considerably from that which occurs in health.

Often absorption is considerably reduced when there is general reduction of vitality; the lower resisting power of the body occurring in chronic constitutional diseases retards absorption. If the intestines themselves are diseased they allow much more rapid diffusion of proteins, toxins and ferments than healthy intestines but absorption of drugs may be adversely affected.

It is not surprising, therefore, that the same drug given to two different patients under similar conditions for the same symptoms, may behave entirely differently, and on testing the urine, one patient may show the presence of the drug and the other may not. The reason of this variation is not far to seek. An analysis of the records of patients admitted into the Carmichael Hospital for Tropical Diseases, Calcutta, showed that in as many as 60 to 70 per cent of patients the gastro-intestinal tract was involved. Detailed investigations revealed that as many as 25 to 30 per cent suffered from helminthic infections, 28 to 30 per cent from catarrhal conditions of the intestines of various origin. The remaining suffered from pathological appendix, gastro-duodenal ulcer, diseased gall-bladder, etc. Helminthic parasites especially hookworm live in the upper part of the small intestine, and even a light infection may alter the normal physiological processes in this part.

In addition to the above, a very large number of patients complained of vague abdominal symptoms although no definite laboratory finding for known infective agents was obtained. Most of these patients showed a condition of hypo- or hyperchlorhydria which is very commonly associated with chronic dysenteries and colitis in which the original causal agent, either bacterial or protozoal, is very difficult to detect. The acidity of the stomach, which is often altered in these conditions, is in itself a factor in the absorption of the drug inasmuch as it is often here that the drug is rendered suitable for absorption by disintegration of tablets and conversion of insoluble into soluble compounds.

Another important factor which should not be lost sight of is that the rapid passage of a drug through the small intestine, where absorption usually takes place, occurs in chronic diarrhoeas and dysenteric conditions. X-ray examinations with barium meal show that the meal in these cases hurriedly passes

through the small intestine, and in a very few hours, less than five usually, it reaches the pelvic colon, no trace being left in the small intestine. Drugs, therefore, are not allowed sufficient time for absorption. Besides these conditions, the mucous membrane of the gastro-intestinal tract is not normal in a large percentage of patients in the tropics, and peptic ulcer, disease of the liver and gall-bladder and pathological appendix, colitis, etc., are frequently met with. The absorption of drugs in such cases may be far from normal and may show considerable individual variations.

Clinical data

The importance of these factors was brought home to us when we were studying the effects of different anti-malarial drugs on patients in the Carmichael Hospital for Tropical Diseases. The results given even with such potent drugs as plasmochin and atebirin were so variable that we were puzzled a great deal at first. It was not till the excretion of these drugs in the urine was studied side by side with their effect on the malarial parasites and clinical symptoms in a series of cases in this hospital that the cause of these discrepancies was understood. A few details about some of these cases may be worthy of attention.

Case 1.—The patient was admitted with a history of periodical fever for three months. He was anæmic and emaciated, and the spleen was enlarged. Examination of blood showed M.T. rings and crescents. Stool examination showed the presence of *Trichomonas hominis*, *E. nana* cysts, *Bact. morgani* and *Bact. para-asiaticus*.

Atebrin 0.1 gm. and plasmochin 0.005 gm. in dragees was prescribed three times a day, but crescents persisted even when the dose of plasmochin was increased to 0.02 gm. twice daily. Usually 0.01 gm. twice daily for two to three consecutive days causes their disappearance. Plasmochin is a toxic drug and even with such large doses as were prescribed no toxic symptoms were produced. The urine tested side by side did not show even traces of these drugs. Normally, they appear in the urine within 36 hours. It was evident, therefore, that no absorption was taking place and therefore parasites remained unaffected. The only effective route for administration in such cases would be parenteral.

Case 2.—The patient was admitted with recurrent attacks of malaria. He was anæmic and somewhat emaciated. The spleen was enlarged 2 inches below the costal margin and was tender. Blood showed scanty M.T. rings. There was a light hookworm infection. Atebrin 0.1 gm. and plasmochin 0.005 gm. were given three times a day but even after their administration for 9 days the parasites and fever persisted. The drugs

could not be detected in the urine till the 10th day of administration when appreciable amounts were found. The parasites then disappeared and the temperature fell to normal.

Case 3.—The patient had a combined M.T. and B.T. infection, and even after the administration of atebirin and plasmochin for eleven days the parasites persisted as also paroxysms of fever. Drugs could not be detected in the urine till the 9th day and then remained in appreciable quantities. This patient had strongly positive W.R. He had a palpable spleen and tender liver.

Case 4.—The patient was a chronic malarial subject and started having attacks of malaria while in hospital. Scanty M.T. rings were found in the blood. The patient also had a heavy hookworm infection. Atebrin and plasmochin were prescribed, but parasites persisted in blood for six days. Only very minute traces of these drugs could be detected in the urine.

Case 5.—The patient had attacks of malarial fever for six days. B.T. rings and growing trophozoites were found in the blood. He had a lot of quinine treatment but with no results. The patient suffered from a chronic dysenteric condition, and organisms of the meta-dysenteric group were found in the stools. Atebrin and plasmochin were given for six days with no results, and later quinine was given but parasites persisted for six days. No atebirin could be detected in the urine. This is the class of case in which gastric acidity is low and the meal rushes through the small intestines.

We could cite many more such cases, but these will suffice to show the effect of disease on the absorption of drugs from the gastro-intestinal tract.

Summary and conclusions

What is true of atebirin and plasmochin holds good in case of other drugs also. Every medical practitioner is familiar with the wide individual variations in response to drugs. No two individuals respond to any drug in an identical manner, and a small minority may react to certain drugs in an wholly abnormal manner. Extensive data in this connection has been gathered from biological standardization of drugs with different stocks of animals and large variations in dosage and response are found. If this is the case with healthy animals, it is not surprising that large variations occur in disease and particularly when the disease affects the gastro-intestinal tract. The physician should carefully consider absorption and excretion of drugs before administering them and when expected results are not forthcoming. From observations entertained over many years in the Calcutta School of Tropical Medicine, the following factors were found to

be responsible for variability in the absorption of drugs from the gastro-intestinal tract. The practitioner in tropical and sub-tropical climates should bear these in mind:—

1. The absorption of drugs is considerably modified in acute and chronic inflammatory conditions of the mucous membrane of the gut.

2. The hypoacidity of the stomach which is often met with in chronic dysenteric and other infections has considerable effect over the absorption of drugs.

3. The rapid passage of meals through the small intestine generally, and through its upper part particularly where these drugs are usually absorbed, hinders absorption. This is quite commonly met with in amœbic and bacterial dysenteries and affections of the liver.

4. The drugs administered in form of tablets may not be properly constituted. Some of the ingredients used may prevent their dis-

integration before reaching the part where absorption of drugs takes place. In some cases the tablets may not disintegrate at all, and may pass through the gut unchanged.

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CORRIGENDA

THE article on 'Serum transfusions in air-raid casualties in South-East Bengal' which appeared in the December 1944 issue, page 611, was an abstract from a lecture given by Lieut.-Colonel K. S. Fitch at the Calcutta Blood Bank.

On page 612—

column 1, line 19—'abdominal and thoracic' should be 'abdomino-thoracic'.

column 2, lines 32-33—'condition is' should be 'condition in'.

On page 613—

column 1, line 8 (from bottom)—'31' should be '39.4'.

Medical News

JOURNAL OF THE INDIAN ARMY MEDICAL CORPS

AN outstanding event of the present war, so far as India is concerned, is the formation of the Indian Army Medical Corps in which officers, warrant officers, N.C.O.s and men have become unified. The new corps has already made a name for itself in the annals of military medical history, and has now started a journal with Colonel D. R. Thapar as editor. We have received a copy of the first issue. The opening article is from Lieut.-General Gordon Wilson, D.M.S. in India, who, as head of the corps, sends a stimulating inaugural message on the occasion. There are articles of professional interest, various corps news and an interesting account of a Field Ambulance in the battle of Cassino, and finally is given a list of honours and awards received by the officers and men together with photos of some of the recipients. We offer a cordial welcome to the new journal. The annual subscription is Rs. 5 and it will be published twice in a year in January and July. The address is Headquarters, I.A.M.C., Poona.

UNIVERSITY OF MADRAS

Council of Post-Graduate Medical Education

A SHORT Refresher Course in modern methods of treatment in Medicine, Surgery, Obstetrics and Gynaecology, and Venereal diseases, open to Medical Graduates and Registered Practitioners, will be held from July to September 1945 in the Madras City hospitals. Further particulars can be had from the

Secretary, Council of Post-Graduate Medical Education, on application, after the 10th of June 1945.

W. McLEAN,
Registrar.

University Buildings,
Chepauk, Madras.
29th May, 1945.

PENICILLIN

THE United States Office of War Information has published a symposium on penicillin containing reprints of twenty-eight articles from various medical journals. After giving a general discussion which includes the story of its discovery, isolation and large-scale production, it describes its use in certain specific illnesses. The last eight articles are devoted to venereal diseases.

HEALTH NOTES*

WE have received a booklet on *Health Notes* by Colonel M. L. Treston, Inspector-General of Civil Hospitals, Burma, Simla, for use by the Government officials. It contains short chapters on personal hygiene, common diseases, public health, maternity and child welfare, diet, town and village planning, etc. Civilians going to Burma will find much useful information in it regarding these subjects. The accuracy of certain statements such as the effect of mepacrine in the treatment of malaria, however, do not appear to be based on modern knowledge.

* Published by the Director of Public Relations, Government of Burma.

Public Health Section

CONTROL OF FLY-BREEDING IN COMPOST HEAPS

By C. N. ACHARYA, D.Sc. (Lond.), F.I.C.
and

K. S. KRISHNA RAO, B.Sc. (Ag.)
Imperial Council of Agricultural Research, Nagpur

IN connection with the large-scale work on composting town wastes that is now in progress at over 200 municipal centres in India, the need has been felt for some simple and effective method whereby fly-breeding could be controlled in manure heaps. The practice of covering the compost mass in trenches or heaps with a layer of earth on the top about 2 inches thick, as adopted in the Bangalore system of composting municipal wastes, helps to prevent oviposition of eggs by outside flies, but does not solve the problem of the destruction of the fly eggs, larvæ and pupæ already contained in the refuse (katchra) or night-soil used for compost-making. The high temperatures of 60°C. and above that are developed in the compost mass, in the dry season, help no doubt to destroy about 50 to 80 per cent of the fly maggots and pupæ contained in the mass, but an appreciable number of larvæ manage to climb up to the top cooler surface of the trenches or sides of the heap and pupate there, and subsequently escape as flies. The trouble is greater in the rainy and cooler parts of the year, when temperatures in the compost mass do not rise to the extent necessary to prove lethal for the maggots and pupæ.

In view of the fact that municipal compost depots are now located quite near to towns, in order to facilitate easy transport of refuse, any possible fly development at the depot is likely to prove a source of danger to the public health of adjoining localities, especially as the refuse (and night-soil) coming to the depot and used for compost-making may contain infected material. It is therefore quite essential for the success of the town composting scheme to see that fly-breeding is completely suppressed at compost depots in all seasons of the year.

Various methods have been recommended from time to time for controlling fly-breeding in manure heaps, e.g. the use of fly traps, fly papers, chemical sprays, thermal methods such as Fay's (1936), use of an electric screen, etc.;

but we have found most of these to be unworkable on a routine basis in compost depots, due either to ineffectiveness of the method employed or to the cost of and difficulty experienced in obtaining the chemicals required. Isaac (1944) recommended applying 3 successive earth plasters, each 4 inches thick on top of the manure heap, but we have found that even a single plaster of 3 inches thickness, though effective if cracking of the surface could be controlled, is impracticable in practice due to the large quantity of earth required, high labour charges involved and the harmful effect which an earth plaster introduces in delaying microbial decomposition of the compost mass.

The Indore process of compost-making (Howard and Wad, 1931) recommends turnings to be given to the mass on the 5th, 12th and 20th day, in such a way as to bring the top surface of the heap to the bottom position at each turning; but in addition to heavy labour and watering charges involved in turnings and the attendant loss of nitrogen and organic matter, we found that unless the turnings are given under skilled supervision, there is considerable scope left for the development of fly larvæ and pupæ in the mass.

We have now evolved a method of fly control, utilizing the principle of asphyxiation of the larvæ and pupæ and any adult flies that may emerge, by subjecting the compost mass to anaerobic treatment for a limited period of one week from the 5th to the 12th day after the compost trench is filled up or the heap is made. The anaerobic treatment is given by covering the top of the trench with a piece of pre-treated hessian, of size a foot greater in length and breadth than the size of the trench. Suitable pieces of hessian (preferably the close mesh type used for packing bales of cloth) may be stitched together so as to give a sheet of the required dimensions to suit the trench in use. The hessian cloth is rendered air-proof in the following manner: the cloth is first smeared on both sides with a thin paste made by mixing together equal volumes of cattle-dung, fine earth and water. After the surface has dried, a second coat is similarly given on each side. This is followed with a good coat of tar given

on both sides; after drying, the surface is dusted over with some fine earth.

The treated hessian cloth is placed on top of the compost trench on the 5th day after the compost is made and the edges of the cloth are fixed well to the ground by placing a 4 inches to 6 inches wide plaster of earth and cattle-dung, mixed in equal volumes, all along the edges of the cloth so that there is plaster below and above the cloth edges. Any cracks that may subsequently form in this plaster along the edges are rectified by smearing with cattle-dung-earth paste; and on the 12th day after the compost was made, *i.e.* after one week of anaerobic treatment, the hessian cloth is removed and used for covering another trench. In the case of overground heaps, a conical cap of hessian, of size sufficient to enclose the compost mass and similarly treated with dung and tar, may be used in a similar manner—the earth plaster in this case being placed all along the bottom edges of the hessian cap.

It has been found that the period, 5th to 12th day, is the most critical period for fly development. Experiments in pits, trenches and heaps fitted with mosquito netting cages on top, with the addition of known counts of fly larval inoculum to the compost mass, at the beginning, showed that: (a) fly emergence started, in general, on the 8th or 9th day after the compost was made and continued till about the 21st or 22nd day; (b) the tarred-hessian cloth method applied during the period, 5th to 12th day, served to bring down fly emergence from a normal level of 40 to 60 per cent of the inoculum count to a low level of 2 to 3 per cent only, indicating an efficiency of over 95 per cent fly control; (c) the capital equipment required, *viz.* 7 or 8 pieces of treated hessian sheets would cost only about Rs. 100 to 150 for a compost depot operating on the basis of one trench per day (20 to 25 feet length and 6 to 7 feet breadth), since the same cloths can be used over and over again, with fresh tarring at intervals; (d) the labour and operating charges are very low and the method could be operated by sweeper labour, without the need for skilled supervision. The extra charges incurred for securing effective fly control by the present method work out to about one anna per cart-load of manure prepared.

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LARVICIDAL FISH OF KANGRA VALLEY—*SCHIZOTHORAX PROGASTUS*

By B. L. RAINA

MAJOR, I.M.S./I.A.M.C.

SEVERAL species of fish have been used for generations to free tanks and pools from mosquito larvæ. Over 50 years ago, Ross noted that certain fish feed on larvæ. Numerous workers (Aitken, 1901; Alcock, 1902; Fry, 1912; Hora, 1927; Graves, 1930; Prashad and Hora, 1936; Covell, 1927 and 1941) confirmed the utility of larvivorous fish in India.

The Top Minnow extensively used in Italy, South America and West Indies, and imported into India about 1929 from Italy and Siam, has established its reputation as a valuable larvicide. Three imported and twenty-two indigenous varieties of fish have so far been described in detail. The three exotics are fairly well known, *viz.* (1) the Top Minnow (*Gambusia affinis*), the most extensively used fish, and distributed free by the various fisheries and anti-malaria centres in India; (2) Gold fish (*Carassius*), the popular ornamental fish imported from the Far East; (3) Barbados Millions (*Sebastas*) used in Ceylon, but could not be acclimatized in India.

The indigenous genera of larvivorous fish include *Aplocheilus*, *Aphanous*, *Anabas*, *Danio*, *Esomus*, *Glossogobius*, *Laubuca*, *Macropodus*, *Notopterus* (probably young ones only), *Ophicephalus*, *Puntius*, *Panchax*, *Rasbora*, *Therapon*, *Trichogaster fasciatus* and *Wallago* (fresh water shark, a very dangerous fish, which should be exterminated).

Hora and Mukerji recommended the following in order of their larvivorous activity: Top Minnow, *Panchax*, *Aplocheilus*, *Aphanous*, *Carprinus* (*Puntius*), *Osphronemus* (*Colisa* and *Macropodus*). Wilson in 1914 suggested *Chela*, *Aplocheilus*, and *Polyacanthus* for paddy fields, wells and ponds, and *Therapon*, *Polyacanthus* for salt and brackish water. Favourable reports have been received about the larvivorous activity of *Barbusphatunio*, *Nuria danrica*, *Ophicephalus*

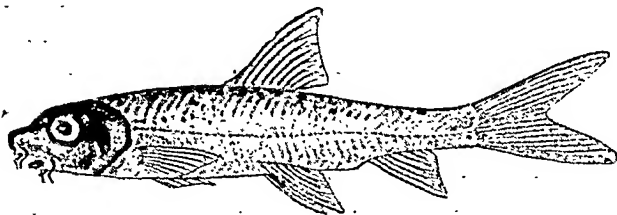
stiatius, *Anabas scandens*, *Hoplochilus*, *Panchax* and *Ophicephalus punctatus* Boc from Jury Valley, Sylhet (Hamilton), and *Trichogaster fasciata*, *Barbus stigma*, *Ambassis nana* and *Barbus ticto* from the Punjab (Bhatte).

Widely divergent views are held regarding the utility of indigenous fish. Hackett (1937) pointed out that 'the local fish after centuries reach a balance regarding to their natural enemies and the number cannot be artificially increased and maintained at an abnormally high level of density whereas if exotic fish can be acclimatized they will proliferate and maintain their number at an abnormally high level'. On the other hand Fry, Prashad, Hora, Sweetin and Meyers advocate the use of indigenous fish and condemn the use of exotic fish on biological grounds.

Schizothorax progastus

During a recent survey of Kangra Valley, it was noticed that a few streams were exceptionally free from mosquito larvæ, whereas at the same height under identical conditions mosquito larvæ were breeding in other streams. After a very careful investigation, no cause could be found except the presence of fish which was later identified as *Schizothorax progastus* by the Director, Zoological Survey of India.

Schizothorax progastus



It has the following characteristics: size $4\frac{1}{2}$ to 6 ins., eyes in the length of the head and situated in its middle. Snout pointed. Depth of the cleft of the mouth equals the width of the gape. Upper jaw projecting. Lips thick and fleshy. Barbels 2 pairs, dorsal fins commence midway between the end of snout and root of caudal fin. Its osseous ray is strong, coarsely serrated and as long as the head behind the angle of the mouth. Scales from 150 to 190 rows along the lateral line, about 18 rows between the lateral line and the base of ventral fin. It is found in rocky hill streams with clear slow running water especially where water is almost 2 to 3 feet deep, with very little vegetation at the edges, and is a very active top feeder. It has been found swimming both singly and in groups. Equally active in dirty water with aquatic and semi-aquatic vegetation. In Yol it does not seem to attain size larger than $6\frac{1}{2}$ inches.

The following investigations were carried out:—

(a) Larvæ were put in a jar full of water. The fish was introduced: 12 larvæ were eaten in one hour and 35 minutes. Next day 12 larvæ were again put: they were eaten in less than 2 minutes.

(b) Equal numbers of larvæ were put in two jars containing in one *Gambusia affinis* and in the other *Schizothorax progastus*. The latter consumed all larvæ in 40 minutes and the former in 3 hours and 25 minutes.

(c) *Gambusia* and *Schizothorax* were starved for 24 hours in separate jars and 12 larvæ introduced in each jar: *Schizothorax* consumed them all in about 2 minutes whereas in the jar with *Gambusia* 10 larvæ were untouched at the end of the same period.

(d) A search was made for natural food of the fish in the stream from where *Schizothorax progastus* was caught, and the following were collected: a few ciliated protozoa, two species of chironomidæ, one species of trichopho nymph, one species of notonectidæ nymph, numerous cyclopodæ, and one species of odonta nymph and two species of dytiscides adults. Twelve larvæ were added to the above collection and *Schizothorax* was introduced. It was noticed that the larvæ were consumed before the rest.

(e) *Schizothorax* was introduced in 12 tanks, 10 feet by 10 feet, and was observed during the malaria season in 1943 and 1944. No breeding of larvæ was found in any tank. Lately the streams have been stocked with success.

(f) *Schizothorax* was dissected and larvæ were found in the gut.

(g) Two dozens of the fish were taken to Lucknow, a distance of over 500 miles. At the end of the journey they were all alive and active.

Conclusion

(i) *Schizothorax progastus* appears to be a valuable addition to the already known larvivorous fish in India.

(ii) It prefers mosquito larvæ to other articles of food available in its natural surroundings. The young ones especially are more actively larvivorous than the adults.

(iii) It is more active (at least under conditions in Yol-Kangra Valley) than *Gambusia affinis*.

(iv) It however suffers from a great disadvantage, being relatively large in size and good for eating.



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(v) It stands transport well, but its habits require further study and investigations before it can be recommended for places other than Kangra Valley.

(vi) Like all larvivorous fish it has its limitation. As suggested by Prashad and Hora (1936) 'for fish to be effective, all vegetable matter and debris that may prevent access of fish to mosquito larvæ should be removed. Disconnected pieces of water separated by short distances should be connected, so as to enable the fish to wander about. Shallow pits and pools should either be deepened, so that the fish may be able to live in them even when the water is at its lowest level in the dry weather and fishing should be strictly prohibited'.

I am grateful to Dr. Bani Prashad, Fisheries Development Adviser to the Government of India, New Delhi, for identifying the fish; Capt. E. H. Eason, R.A.M.C.,

for carrying on the dissection; Major A. Guidicini, for drawing of the fish; and Mr. Kher Sing, for his keen painstaking observation and collecting useful materials.

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Current Topics

Copper Sulphate Method for Measuring Specific Gravities of Whole Blood and Plasma*

By R. A. PHILLIPS

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K. EMERSON

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WITH THE TECHNICAL ASSISTANCE OF

E. G. STANLEY

and

J. PLAZIN

(Abstracted from the *U. S. Army Medical Bulletin*, December 1943, No. 71)

PRINCIPLE OF THE METHOD

THE technique consists of letting drops of plasma or whole blood fall into a graded series of solutions of copper sulphate of known specific gravity, and noting whether the drops rise or fall in the solutions. Each drop on entering the solution becomes encased in a sack of copper-proteinate, and remains as a discrete drop without change of gravity for 15 or 20 seconds, during which its rise or fall reveals its gravity

relative to that of the solution. The size of the drops does not have to be constant, hence no special pipette is needed for delivering the drops. No temperature correction is needed, because the temperature coefficient of expansion of the copper sulphate solutions approximates that of blood and plasma. This method is capable of measuring gravities to ± 0.00005 which is more than ten times the accuracy required. The copper sulphate solution automatically cleans itself after each test, because within a minute or two after the test is completed the material of the drop settles to the bottom as a precipitate. The standard CuSO_4 solutions are prepared by dilution of a saturated solution, hence a balance is not needed to weigh the CuSO_4 .

The principle of dropping blood into a series of solutions of known gravity has been applied for decades but has never achieved entire success. Mixtures of organic liquids have been used, e.g. benzene and chloroform, but they were liable to change in specific gravity due to differential evaporation of the components. They also have temperature coefficients of expansion several times that of water or blood and cannot be used without accurate temperature regulation. In addition, some of them give rise to toxic and to explosive vapours. Dispersion of blood occurs too rapidly in the usual aqueous salt or glycerol solutions to enable small gravity differences to be measured easily and accurately. The use of aqueous standard solutions which have protein-coagulating power overcomes these difficulties.

For accurate work, viz, gravities within ± 0.0002 , a series of copper sulphate solutions graded at intervals of 0.001 in specific gravity is used; twenty solutions

*This article was published in the *U. S. Army Medical Bulletin*, December 1943, but is not available to us in the original. The abstract printed here was received from Dr. Janet Vaughan, Medical Officer-in-charge, N. W. London Blood Supply Depot, The Social Centre, Farnham Road, Slough, Bucks. This method of blood analysis is discussed in an editorial on page 265.

cover the plasma range 1.015-1.035 and forty cover the whole blood range, 1.035-1.075 for rougher work with gravities accurate to ± 0.001 , sixteen solutions at intervals of 0.004 suffice to cover the entire range of blood and plasma.

Plasma gravity is best determined on plasma from blood which is treated with heparin, 0.2 mg. per c.c. blood, as anticoagulant, since the heparin exerts no measurable effect on the gravity results. Almost equally good is Heller and Paul's mixture of 3 parts ammonium oxalate and 2 parts potassium oxalate if the amount used does not exceed 1 mg. per c.c. of blood.

Sodium citrate cannot be used as anticoagulant. In effective concentrations it exerts too great an effect on the gravities.

Serum may be used in place of plasma, with a slight correction indicated under 'Calculations' for the effect of fibrinogen removal on the gravity.

DETERMINATION OF GRAVITY

The drop of serum, plasma or whole blood is delivered from a height of about 1 cm.* above the solution from a medicine dropper, or from a syringe needle. It is preferable to use small drops for the reason that they permit more tests before the standard solution must be changed. Therefore a medicine dropper with a fine tip is preferable to a coarse one. Greasing the sides of the tip with vaseline also reduces the size of the drop, especially if the vaseline is mixed with a little caprylic alcohol. When the drop is delivered it is convenient to steady the dropper on the edge of the bottle.

The delivered drop breaks through the surface film of the solution and penetrates 2 to 3 cm. below the surface: within 5 seconds the momentum of the fall is lost and the drop then either begins to rise, or becomes stationary, or continues to fall. The gravity of the drop relative to the solution does not change appreciably until the drop has been immersed in the solution for another 10 or 15 seconds, and there is ample time to note its behaviour during this interval. If the drop is lighter than the test solution it will rise, perhaps only a few millimetres, and may begin to sink immediately afterwards. If the drop is of the same gravity as the standard test solution it will become stationary for this interval and then fall. If the drop is heavier it will continue to fall during the interval. *In summary, the behaviour during the 10 seconds after the drop has lost the momentum of its fall into the solution indicates whether the drop is lighter or heavier than the test solution: if it rises at all during this period it is lighter than the standard.*

CALCULATIONS

Use of line charts

Line charts for the conversion of plasma and whole blood gravities to plasma protein concentrations, hæmo-

globin concentrations and hæmatocrit percentages have been prepared by standard methods and are given at the end of this article.

The calculations are made by laying a straight edge or stretched thread as directed on the charts. The brackets on the scales indicate normal ranges.

Corrections to observed gravities for the effects of addition of oxalates or removal of fibrinogen.—Addition of oxalates raises the gravity of whole blood and of plasma: on the other hand removal of fibrinogen by clotting when no anticoagulant is used yields serum, which has a gravity lower than that of plasma. These effects are so small that for clinical studies the errors introduced may ordinarily be neglected, and figures for plasma proteins and hæmoglobin may be calculated with sufficient accuracy by applying the observed gravity values of blood and plasma or serum directly to the line charts. However, if more than 1 mg. of oxalate mixture per c.c. of blood is used, or if the greatest precision is desired, corrections are applied as follows:—

Corrections for added anticoagulants.—No corrections are needed if heparin 0.1 or 0.2 mg. per c.c. of blood is used.

For each mg. of the ammonium-potassium oxalate mixture added per c.c. of blood subtract 0.0004 from the observed G_{B} and the observed G_{P} . If a tube prepared with 5 mg. of oxalate receives the expected 5 c.c. of blood, the correction to G_{P} and G_{B} is therefore 0.0004. Neglect of the 0.0004 correction would lead to an over estimation of the plasma proteins by 0.1 gm. per 100 c.c. of plasma, and of hæmoglobin by 0.1 gm. per 100 c.c. of blood, errors which may usually be neglected.

If, however, the volume of blood placed in the tube is less than 5 c.c. the oxalate concentrations will be greater, and the corrections to G_{B} and G_{P} will be as follows:—for 4 c.c. of added blood — 0.0005: for 3 c.c. — 0.0007: for 2 c.c. — 0.0010: for 1 c.c. — 0.0020.

Correction when serum is used in place of plasma.—The serum gravity indicates correctly the serum protein, but not the plasma protein, which is higher by the 0.2 gm. or more of fibrinogen per 100 c.c. present in the plasma.

If the uncorrected serum gravity is used as G_{P} to calculate hæmoglobin from G_{P} and G_{B} , the calculated hæmoglobin value will exceed the correct value by about 0.1 gm. per 100 c.c., because the difference between whole blood and plasma gravities, on which the hæmoglobin calculation is partly based, is slightly exaggerated by removal of the fibrinogen.

If no anticoagulant is used, and serum gravity is determined after clotting, the plasma gravity may be estimated by adding 0.0005 to the observed serum gravity.

NUMBER OF ANALYSES THAT CAN BE MADE BEFORE RENEWAL OF THE COPPER SULPHATE SOLUTION IS NECESSARY

Tests have shown that a standard solution will receive about one-fortieth its volume of plasma or blood, or one small drop per c.c. under the conditions of the tests before the gravity of the standard is changed by 0.0005. The change is to decrease the gravity. A 4-ounce bottle of standard serves for about 100 tests:

*If the drop falls from too great a height it may be broken up on striking the solution, or its momentum may carry it too far below the surface. On the other hand if it strikes with too little force the drop may not break through the surface film. A fall of about 1 cm. gives the right striking force.

When whole blood is tested in the copper sulphate solution some hæmolysis occurs, the colour of the solution shifts from blue towards green, and it becomes slightly turbid from suspended unlaked cells. However, the gravity of the solution is not changed by more than 0.0005 until one-fortieth its volume of blood has been added.

In order to tell when the solutions in the bottles should be changed prepare for comparison two extra standard solutions of gravity about 1.028 and 1.060 in the same sized bottles. To the solution of gravity 1.028 add one-fortieth its volume of normal plasma and to the solution of gravity 1.060 add one-fortieth its volume of normal whole blood. These control bottles are kept for comparison with used standards. When the volume of precipitate in the bottom of a standard equals that in the control bottle the standard is renewed.

If for any reason, it is impossible to renew the standard solutions after they have been used often enough to decrease their gravity by 0.0005, the standard may be re-labelled with a gravity of 0.0005 lower and used further. Thus, after 50 small drops have been added to 50 c.c. of a 1.028 standard in a 2-ounce bottle, the standard can be re-labelled 1.0275. (The authors do not feel that this is a desirable procedure, but it may be resorted to in an emergency.)

A standard of 25 c.c. volume should be replaced after about 25 tests. However, a complete set of standards varying by 0.001 can be used for many more than 25 tests since each standard will not be used in every test.

REAGENTS

Oxalate mixture.—Three gm. ammonium oxalate and 2 gm. potassium oxalate are dissolved in 250 c.c. H_2O to make a 2 per-cent oxalate solution.

This oxalate mixture, suggested by Heller and Paul, disturbs cell and plasma gravities less than either potassium or ammonium oxalate alone.

Crystalline copper sulphate, $CuSO_4 \cdot 5H_2O$.—This is preferably purchased in the form of 'fine crystals'. Otherwise it must be pulverized before using. Four pounds provide a complete set (70) of 100 c.c. standard solutions. Ten pounds will probably suffice a laboratory for a year.

Saturated copper sulphate solution.—This solution is used to prepare a stock solution of gravity 1.100 ± 0.0003 . Use of a solution saturated at a known temperature affords a precise means of preparing the stock solution without a balance. The saturated solution is prepared as follows:—

Four pounds of 'fine crystals' or pulverized copper sulphate are placed in a 4-litre bottle. About 2,500 c.c. of distilled water* is added and the bottle is stoppered and shaken vigorously for a total of 5 minutes, which need not be continuous. (Three minutes have been found sufficient, even at $0^\circ C.$, to saturate this solution if the sulphate is well pulverized.) As soon as the

shaking is finished the temperature of the solution is taken to the nearest half degree centigrade and is recorded. (It will be a little cooler than the water was before the saturation, because the saturation process absorbs heat.) After taking the temperature the solution is *immediately* decanted off the crystals and is filtered, to remove fine suspended crystals, through cotton or dry filter paper into a clean dry 4-litre bottle. The solution is at once used to make up a stock solution of gravity 1.100. (It is preferable not to let the saturated solution stand long before using, as if it cools some of the copper sulphate may crystallize and change the concentration.) The undissolved sulphate can be used again.

Two and a half litres of the saturated solution suffice for more than 4 litres of the stock solution of gravity 1.100 and this in turn is sufficient for a complete set of 70 standard solutions of 100 c.c. volume each, with enough surplus to provide replacements for the standards which are most used. Smaller or larger amounts of the saturated solution can be made by using proportional amounts of copper sulphate and water.

Stock copper sulphate solution of gravity 1.100.—(Gravity figures in this report were determined as the ratio of the weight of copper sulphate solution to the weight of an equal volume of water at the same temperature.) The volume of saturated solution is measured in a 500 c.c. graduated cylinder and poured into a 1-litre volumetric flask. The upturned cylinder is allowed to drain into the flask for 30 seconds. The flask is then filled to the mark with water, and is inverted several times to mix the solution. The mixing results in a contraction, so that the meniscus now falls below the mark. The flask is let stand for a minute until the solution drains down from the neck. Then enough additional water is added to bring the volume to 1 litre, the solution is mixed and then poured into a clean, dry 4-litre bottle. The same 1-litre volumetric flask is used to prepare 3 more litres of the stock copper sulphate solution of gravity 1.100. Each time before the flask is used again it is rinsed with water and the rinsings are discarded.

The saturated solution, the stock solution and the standard solutions next described must be prepared at within $5^\circ C.$ of the same temperature. The coefficients of expansion of the saturated and stock copper sulphate solutions are slightly but definitely greater than that of water, so that if, for example, the saturated solution and stock solution were prepared at $35^\circ C.$, and the standard solutions at $20^\circ C.$, the standards would have more copper sulphate than intended, enough to increase the gravity by about 0.001.

Once prepared, the standard solutions may be used at any temperature within $\pm 15^\circ$ or 20° of the temperature at which they were made up.

The accuracy of the stock solution of gravity 1.100 can be checked by weighing 100 c.c. in a volumetric flask, and then weighing 100 c.c. of distilled water at the same temperature in the same flask. The copper sulphate solution should weigh 1.1000 times the weight of the water. This check is not necessary unless unusual precision for special purposes is desired.

Alternative preparation of stock solution of gravity 1.100 by weight.—Weigh 159.63 gm. of crystalline

* Rain water or tap water of gravity not more than 1.0003 compared to distilled water at the same temperature as 1.0000 may be used in place of distilled water for preparing the saturated stock and standard solutions.

$\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$. Place in 1-litre flask with about 800 c.c. of water. Warm and swirl contents till solution is complete. Cool to 20–25°C. Make up to 1 litre with water.

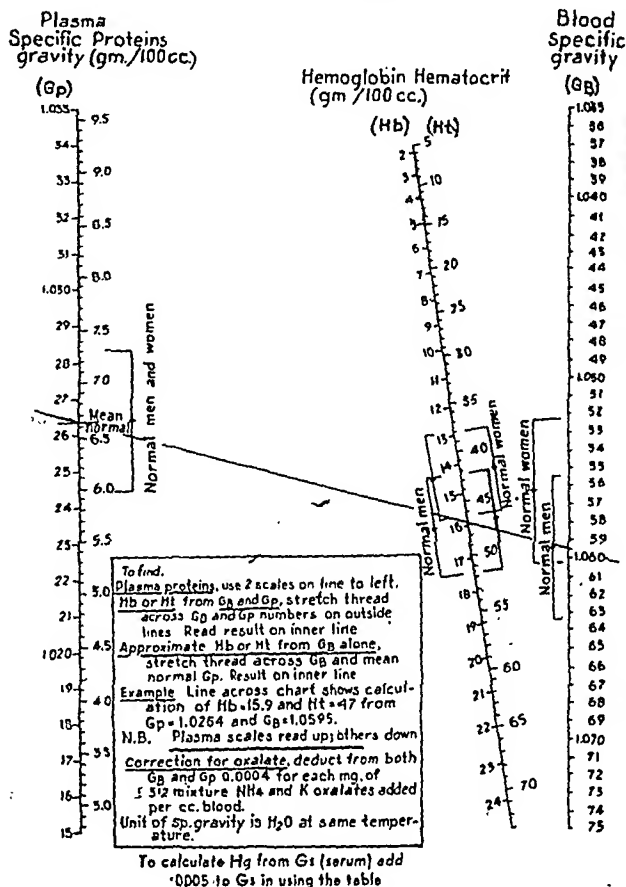
Preparation of standard solutions in 100 c.c. portions.—The standard solutions are prepared in 100 c.c. portions when 4-ounce bottles are available for storage.

For the standard of 1.075 gravity, 74 c.c. of stock solution of gravity 1.100 are measured from the burette into the 100 c.c. flask, the flask is filled to the mark with water, and the solution is mixed and transferred to a labelled 4-ounce bottle which is stoppered to prevent evaporation.

To prepare the standard of gravity 1.074 the 100 c.c. flask is rinsed once with water and the burette is refilled from a 250 c.c. Erlenmeyer flask containing the stock solution. Then 73 c.c. of the stock solution are measured into the volumetric flask and diluted to 100 c.c.

The same procedure is carried through for preparation of the entire series down to 1.015, which covers the extreme ranges for blood and plasma. If gravities on ascitic fluid and transudates are desired, the series is extended to 1.008. For each standard the number of

Line chart for calculating plasma proteins, hemoglobin and hematocrit from gravities of plasma and blood.



c.c. of stock solution less by 1 than the number indicated in the second and third decimal places of the desired gravity is measured into the rinsed 100 c.c. flask and diluted to the mark.

If there were no contraction when the stock solution is mixed with water one would dilute 75 c.c. of the stock to 100 c.c. to get a gravity of 1.075, etc. However, there is a contraction which is empirically corrected for by taking 1 c.c. less of the stock. It happens conveniently that the same 1 c.c. correction serves for the entire range, 1.075 to 1.008 over which its use yields gravities correct within ± 0.0003 .

If, for purposes of special precision, gravities exact to 0.0001 are desired the standards could be made up accordingly. However, the convenient rule of thumb, outlined above, of taking 1 c.c. less than indicated by the decimal figure of the desired gravity, suffices for ordinarily required accuracy.

Preparation of standard solutions in 50 or 25 c.c. portions.—If it is preferable to prepare only enough of each standard to charge a test-tube or a 1- or 2-ounce bottle, portions of 25 or 50 c.c. are prepared by dilution of the volumes indicated to 25 or 50 c.c. in volumetric flasks of these capacities. The burettes used are likewise of 25 or 50 c.c. capacity.

For the field set for approximate plasma and blood analyses, sixteen standard solutions covering the range 1.016 to 1.076 in steps of 0.004 are prepared.

For the pocket field set for whole blood only, six standard solutions of gravities 1.040, 1.046, 1.052, 1.058, 1.064 and 1.070 are prepared in 1-ounce bottles.

The Geographical Distribution of Mite-Borne Typhus Fever

By J. F. CORSON, O.B.E.

and

C. WILCOCKS

(Abstracted from the *Tropical Diseases Bulletin*, Vol. IXL, June 1944, p. 431)

INDIA

THE mite-borne type of typhus fever has been found in the Simla Hills, Madras and Bombay. Woodhead and Dutta examined sera from various parts of Assam where no typhus fever has hitherto been reported. They used *Proteus* OX19, OXK and OX2 and found that 8 out of 203 sera gave diagnostic titres with OXK, one agglutinated at 1/3,500, another at 1/800 and a third at 1/550.

Boyd found 43 cases whose sera gave preponderating agglutination with *Proteus* XK; of these 35 were clearly defined, 21 being British and 14 Indian. He mentions the following localities:—

Districts—Lahore (15 cases), Meerut (5), Bengal and Assam (6), Deccan (8), Burma (1).

Stations—

British—Kasauli, Calcutta, Dagshai, Sabathu, Chakrata, Dinapore, Jhansi, Mingaladon.
Indian—Bareilly, Alipore, Jubbulpore, Trimulgherry, Lansdowne.

There was no evidence of mite-transmission.

Bush recorded six cases, four British and two Indian. He gives the following localities in the Simla Hills:—Solon, Dagshai, Kasauli, Nalwa (near Kasauli).

Macnamara described an epidemic in the Simla Hills Stations—Sabathu, Dagshai and Kasauli. No vector or reservoir was found.

At the King Institute, Guindy, Madras Presidency, out of 4,381 sera examined, 16 gave a positive result with *Proteus* OXK at a titre of 1/200 or more. No virus was isolated. In the 1936 report the sera of 66 out of 134 squirrels examined were positive to OXK in dilutions of 1/25 to 1/200.

Bombay

Patel found that the serum of one out of six cases of typhus fever was positive to OXK at 1/1,500 dilution.

Progress in the Treatment of Typhus Fever and of Rocky Mountain Spotted Fever

(From the *Journal of the American Medical Association*, Vol. CXXVI, 9th December, 1944, p. 964)

THE conditions caused by specific rickettsias, such as typhus and Rocky Mountain spotted fever, present striking ætiologic, pathologic and clinical similarities. The course and the symptoms result largely from the widespread localization of the rickettsial organisms in the vascular endothelium. In a detailed study of the circulation in severe epidemic typhus in French Morocco, Woodward and Bland obtained evidence that circulatory collapse in typhus is mainly peripheral in origin and not due to primary cardiac failure. They demonstrated reductions in the blood volume and in blood proteins, especially albumin, and other alterations, all of which are explainable as due to the vascular lesions of typhus and increased capillary permeability. Emphasis is placed on the importance of general supportive measures to restore the volume and the quality of the blood. Harrell and his co-workers have pointed out that supportive measures are not used as much as they should be in the treatment of Rocky Mountain spotted fever. They too emphasize the loss of volume and of proteins by the blood on account of the vascular lesions which may lead to peripheral circulatory collapse if the proper treatment is not given. Yeomans and others have reported on the effect of para-aminobenzoic acid in epidemic typhus in Cairo, Egypt. Under well-controlled conditions they compared the clinical course of 20 treated cases with that of 44 control cases. Beginning with 4 to 8 gm. of para-aminobenzoic acid by mouth, 2 gm. was given every two hours or enough to maintain the concentration of the acid in the blood between 10 and 20 mg. per hundred cubic centimetres until the rectal temperature remained at 99.5°F. or less for twenty-four hours. These amounts were taken with ease by the patients and without any serious untoward effects. In patients who received the acid in the first week of illness, the course of the attack was much less severe and considerably shorter than in 'untreated' patients. The fact that para-aminobenzoic acid may have curative effect in human as well as in mice typhus directs attention to many problems for investigation. What effect will para-aminobenzoic acid and related compounds have on Rocky Mountain spotted fever and other rickettsial diseases?

Slide Agglutination Test for Rapid Diagnosis of Pre-Eruptive Typhus Fever

By A. A. SMORODINTZEFF

and

R. V. FRADKINA

(From the *Proceedings of the Society for Experimental Biology and Medicine*, Vol. LVI, June 1944, p. 93. As abstracted in *Tropical Diseases Bulletin*, Vol. IXL, December 1944, p. 1021)

THE practical application of this test is based on the observation of Drobyshevskaya and Smorodintzeff (*J. Epid. and Microbiol.*, Moscow, 1942, No. 1) that a specific antigen occurs in the serum of patients during the first few febrile days of typhus fever. About 60 per cent of 107 typhus patients studied during the pre-eruptive stage had enough antigen to be detected by the complement-fixation test, and the antigen was absent from sera of 57 patients with typhoid, dysentery and pneumonia. The specific antigen could no longer be detected after the sixth to the ninth day when antibody appeared.

The technique described in the paper was devised as a simple method of demonstrating the presence of the antigen in the early stages of attacks of typhus fever. The results obtained by this simple and rapid slide test were found to be comparable with those of the complement-fixation test.

Chemically-pure carmine is finely ground in a mortar and is made into a 2 per cent suspension by the gradual addition of distilled water while the carmine is being constantly triturated. After shaking the mixture for 10 minutes in a vessel with glass beads the larger particles are removed by a short period of slow centrifugation. The suspension is then kept for 24 hours, then centrifuged to precipitate most of the carmine particles. After decanting the supernatant fluid the sediment is resuspended in the original volume of 0.25 per cent solution of NaCl.

Serum to be tested (finger blood, lysed in distilled water, can also be used) is diluted 1 to 5 with distilled water and one-quarter volume of the carmine suspension is added. The mixture is shaken for 5 to 10 minutes, then lightly centrifuged (500 r.p.m. for 5 minutes); most of the supernatant fluid is decanted and the sediment is resuspended in the residual fluid. Such antigen-laden particles of carmine are specifically agglutinated by the human serum rich in antibody, but the intensity of the reaction is increased several-fold if the antibody is used not as such, but also absorbed on particles of carmine. 'In the actual test, two drops of the suspension of carmine, laden with serum collected during the acute phase of the disease (antigen), are placed separately on a glass slide. To one of them is added a drop of a suspension of carmine particles laden with antibody-containing serum; to the other, as control, is added a suspension of particles to which negative serum was absorbed.' Agglutination becomes visible macroscopically within a few minutes.

Solutions with low concentration of electrolytes must be used; even so, certain lots of carmine are unusable because of non-specific aggregation.

Sera should be used within five days.

Weil's Disease in Normandy : Its Treatment with Penicillin

By E. BULMER

(Abstracted from the *British Medical Journal*, i, 27th January, 1945, p. 113)

I HAVE presented the results of the treatment with penicillin of 16 cases of Weil's disease. It would appear that there has been an effect on the speed with which the temperature falls and on the number of febrile relapses, while all the observers claimed an improvement in the patient's general condition within 36 hours. These are scanty pieces of evidence on which to base definite conclusions.

In another theatre of war penicillin treatment, in my opinion, has been considered as ineffectual, but the dosage used was inadequate—15,000 units 3-hourly. It is known that certain strains of leptospira are penicillin-sensitive *in vitro*.

In view of these facts it is felt that further work on this subject should be pursued; it is essential to give treatment early, and the dosage should be high.

The Cephalin-Cholesterol Flocculation Reaction as a Test of Hepatic Function

By A. DICK

(Abstracted from the *British Medical Journal*, i, 10th February, 1945, p. 182)

THE cephalin-cholesterol flocculation test is an entirely empirical reaction, but is simply carried out and appears to be of value as a test of hepatic efficiency.

Positive flocculation occurs in the presence of a parenchymatous disease of the liver, and the degree of flocculation runs parallel with the severity of the case. A persistently positive flocculation is an unfavourable sign.

The test is of value in the differentiation of jaundice due to infective hepatitis from that due to biliary obstruction.

It is useless as a test in the early detection of liver damage in arsenical jaundice.

The test is positive in a small number of patients whose illnesses are not known to affect the liver; in normal healthy individuals, however, it is always negative.

From my experience the test is of definite value, even although its mechanism is not understood.

Reviews

DISEASES AFFECTING THE VULVA.—By E. Hunt, B.A., M.D., Ch.B. (Liverpool). Second Edition. 1943. Henry Kimpton, London. Pp. 211, with 38 illustrations and 18 plates in colour. Price, 21s.

THIS is the second edition of a small handbook intended for the gynaecologist and general practitioner on the subject of vulval affections. It is written from the standpoint of a dermatologist. Considerable space is given to seborrhoeic conditions and lichen planus, and these conditions are illustrated by coloured plates.

Veneral diseases are treated very shortly and the treatment of syphilis is omitted. One finds no reference to the ulcerating granuloma of the pudenda which is met with in the tropics and which responds to antimony and sulphonamide treatment.

The main value of the book lies in the details of medical treatment which the author has found effective in her own experience. There is a bibliography at the end of each chapter.

M. I. N. E.

BOOKS RECEIVED

1. The rehabilitation of the injured : Occupational therapy, by J. H. C. Colson. Published by Cassell and Co., Ltd., London, 1944. Price 15s.

2. Casualty work for advanced first-aid students, by A. W. Macquarrie, M.B., Ch.B. (Edin.). Published by E. and S. Livingstone Ltd., Edinburgh, 1944. Price 4s. 6d.

3. Minor Surgery. Edited by Sir Humphry Rolleston, Bt., G.C.V.O., K.C.B., M.D., F.R.C.P., and Alan Moncrieff, M.D., F.R.C.P. Published by Eyre and Spottiswoode (Publishers) Ltd., London, 1943. Price 16s.

4. Diseases of the nose, throat and ear : A handbook for students and practitioners. By I. Simson Hall, M.B., Ch.B., F.R.C.P.E., F.R.C.S.E. Third edition, 1944. Published by E. and S. Livingstone Ltd., Edinburgh. Price 15s.

5. Recent advances in anaesthesia and analgesia (including oxygen therapy), by C. Langton Hewer, M.B., B.S. (Lond.), D.A. (Eng.). Fifth edition, 1944. Published by H. K. Lewis and Co., Ltd., London.

6. Lumbo-sacral strain : A handbook on its relief and cure, by manipulation therapy, by B. H. Vincent Langley, 1944. Published by Research Books Ltd., London. Price 6s.

7. Birth control for the millions, by Santosh Kumar Mukerji, M.B. 1944. Published by Medical Book Co., Calcutta. Price Rs. 4-8.

8. An introduction to physical methods of treatment in psychiatry, by William Sargent, M.A., M.B. (Cantab.), M.R.C.P., D.P.M., and Eliot Slater, M.A., M.D. (Cantab.), M.R.C.P., D.P.M. 1944. Published by E. and S. Livingstone Ltd., Edinburgh. Price 8s. 6d.

9. Aids to theatre technique, by M. Houghton, S.R.N., S.C.M., D.N., and M. Harding, S.R.C.N., S.R.N., S.C.M. 1944. Published by Baillière, Tindall and Cox, London. Price 4s.

10. Elementary anatomy and physiology, by James Whillis, M.D., M.S., F.R.C.S. Second edition, 1944. Published by J. and A. Churchill Ltd., London. Price 15s.

11. Surgical epitome, by D. V. Nadkarni, M.S. (Bom.), F.R.C.S. (Eng.). Vols. I and II. 1944. Published by N. M. Tripathi Ltd., Bombay. Price Rs. 24.

12. Psychology and psychotherapy, by William Brown, D.M. (Oxon.), D.Sc. (Lond.), F.R.C.P. Fifth edition, 1944. Published by Edward Arnold and Co., London. Price 14s.

13. Your food : A study of the problem of food and nutrition in India, by M. R. Masani. Published by Padma Publications Ltd., Bombay. Price Re. 1.

14. Recent advances in therapeutics (parts I and II), by J. R. Goyal, M.B., B.S. Second edition, 1944. J. R. Goyal, Delhi. Price Rs. 6-8.

15. The hair and scalp: A clinical study (with a chapter on hirsuties), by Agnes Savill, M.A., M.D. (Glas.), F.R.C.P.I. Third edition, 1944. Edward Arnold and Co., London. Price 16s.

16. Murrell's what to do in cases of poisoning, by Harold G. Broadbridge, M.B., B.S. (Lond.). Fifteenth edition, 1944. H. K. Lewis and Co., Ltd., London. Price 8s.

17. Functional disorders of the foot: Their diagnosis and treatment, by F. D. Dickson, M.D., F.A.C.S., and R. L. Direley, A.B., M.D., F.A.C.S. Second edition, 1944. J. B. Lippincott and Co., London. Price 30s.

18. Essentials of dermatology, by Norman Tobias, M.D. Second edition, 1944. J. B. Lippincott and Co., London. Price 28s.

19. Essentials of industrial health, by C. A. Sappington, M.D., Dr.P.H. 1943. J. B. Lippincott and Co., London. Price 42s.

20. Practical bandaging including adhesive and plaster of paris dressing, by Eldridge L. Eliason, A.B., M.D., S.C.D., F.A.C.S., F.I.C.S. Sixth edition, 1943. J. B. Lippincott and Co., London. Price 10s. 6d.

Abstracts from Reports

CORRECTIONAL AND REHABILITATION WORK (JUVENILE JAIL, BAREILLY, 1939-1944)

We have received a summary of the work done in the Juvenile Jail, Bareilly, which receives boys convicted for the first time, only on transfer from other jails. Its psychiatric approach to delinquency is of interest. The boys are made to feel at home, their time and mind are kept occupied, and eventually the habit of work is created in them. Selected boys are employed in factories outside and their wages are mostly credited to their account. Thus during a period of 5½ years 241 boys had such employment with only one escape. Many have been trained in trade or profession inside the jail and allowed to do private work, while four bright ones have been put in a local school. Financial help is given to the deserving boys, and the Juvenile Jail Boys Fund is maintained.

Correspondence

ON THE D.E.C. MEDIUM OF PANJA AND GHOSH

SIR,—While the opportunity to examine stool specimens for cholera vibrios is very rare in America, there is a great demand for plating media with a broad range, i.e. on which all pathogenic members of the 'enteric' group grow abundantly and in easily agglutinable colonies, but on which non-pathogenic organisms, mainly colon bacilli and Gram-positive microbes are checked. The S.S. agar nearly fulfils these requirements, except that *Sh. dysenteriae* Shigae, some *Sh. sonnei* strains and fastidious members of the genus *Salmonella*, as *S. paratyphi* A, *S. sendai*, etc., are not always easy to cultivate on this medium.

Additional difficulties were experienced when colonies grown on S.S. agar were used for direct slide agglutination tests. Finally, some workers prefer cheaper, home-made media to desiccated, more expensive market products. Thus we became much interested in the new plate described by Panja and Ghosh in this journal (Vol. LXXVIII, No. 1, Jan. 1943, p. 43) and examined it. While detailed results of our studies will be published in the U.S.A. and in South America, we also wish to record our experiences in a journal that is more easily accessible to the medical circles of India.

Due to wartime difficulties in securing chemicals from other countries, sodium taurocholate (Smith Stanistreet and Co. in the original prescription) had to be substituted with a proper amount of sodium desoxycholate (0.40 per cent, according to the latest tests). Peptone 'Defco' was substituted with Proteose-Peptone + 3 'Difco'. The addition of a small amount (0.20 per cent) of a 0.40 per cent watery solution of brom thymol blue rendered the colour change of the colonies sharper.

All seven *V. cholerae* strains and one *V. El Tor* strain of our collection grew well on the D.E.C. plate. *Shigella* and *Salmonella*, including fastidious organisms, such as *Sh. dysenteriae* Shigae (3 strains), *Sh. sonnei* (one S.S.-resistant strain), *S. paratyphi* A (3 strains), *S. sendai* (2 strains), *S. pullorum* (2 fastidious strains), *S. typhi-suis* (1 strain) and 3 *Sh. paradyenteriae* strains which were difficult to grow on S.S. agar showed no inhibition on the D.E.C. plate. All pathogenic organisms that were easy to cultivate on S.S. medium, grew well on the D.E.C. plate. About one hundred *Salmonella*, *Shigella* and typhoid strains were tested to date on Panja's and Ghosh's medium, with excellent results.

The D.E.C. plate is being introduced for diagnostic use and the preliminary reports are very encouraging.

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THE IMMEDIATE NEED OF REFORM OF THE MEDICAL COUNCILS OF INDIA

SIR,—My object in writing this letter is to bring to the notice of the medical men of this country the main defect of our medical councils. The defect has existed from the very inception of the medical acts despite my earnest efforts to have it rectified. The defect has now been discovered during the G.M.C. versus Spakeman Appeal Case 1943, p. 627. The decision in this case has naturally made the G.M.C. realize its status with regard to its procedure. We in this country can hardly ignore the decision.

The first Medical Act in England was passed in 1858 with a view to registering all qualified medical

mén. Then a body now known as General Medical Council was set up to regulate registration. Its main function now is registration of medical students and doctors. It recognizes various qualifications for additional registration. The Dentist's Act is also in force.

In India the medical councils did not come into existence until about the early part of the nineteenth century, between 1912 and 1915. The All-India Medical Council was set up only recently in New Delhi. The functions of the medical councils in India are almost identical with those in England, but they do not register medical students. They appoint medical examiners to inspect various colleges of the universities and schools to see that a proper standard of medical education is kept up. But the main function is registration and erasing the names of the doctors for various offences. Many times during the term of my office I had to question the council as to the procedure adopted in tackling a case of professional misconduct, etc. The councils usually stick to their guns, and this results in great injustice to doctors and sometimes the councils ignore any heed given to them.

The facts of the above-mentioned case are that Mr. Spakeman had been cited as co-respondent in a Divorce Court. The Court found him guilty of having committed adultery with a woman who was his patient. The G.M.C. notified him (our councils do likewise) that it was about to decide whether his name should be removed from the medical register pursuant to section 29 of the Medical Act, 1858, which provides that if, any registered medical practitioner shall be convicted of any felony or misdemeanour or after due enquiry be judged guilty of infamous conduct in a professional respect, etc., his name will be removed from the register. The respondent applied to the G.M.C. for permission to call for certain evidence which had not been before the Divorce Court although he admitted it would have been available then. The council refused to admit evidence and directed his name to be erased from the medical register. The case after passing through the King's Bench Division eventually reached House of Lords where the appeal of the G.M.C. was dismissed unanimously. Viscount Simon pointed out that after 'due enquiry' in the Medical Act meant due enquiry by the council. Although the council was entitled to treat the conclusion reached in the Divorce Court as *prima facie* proof of the matter alleged, it must permit the doctor to challenge the correctness of the decision. In criminal cases it is conclusive, but an infamous conduct can only be found on due enquiry and as the council refused to admit further evidence there had been no enquiry.

Many interesting points have arisen from this. In the first instance the G.M.C. considers itself ill-qualified on such a charge. Secondly, the council found that it could not administer an oath to witnesses who appear before it. Besides the above two points Lord Atkin held that this appeared to ignore the provisions of the Lord Brougham's Evidence Act, section 16.

It would be clear now that the position of our medical councils is in no way better than that of the General Medical Council.

I hope that all the medical men in India as well as the Indian Medical Association and other powerful bodies will at once take up the question of redrafting the medical constitution. The help of the best legal luminaries should be sought to make it as perfect as possible. A small committee of about seven members or more selected from amongst the best medical men and legal men may be set up to review and redraft all the Medical Acts including the All-India Medical Act.

RAJINDER SINGH GREWAL,
Additional Civil Surgeon.

COMILLA,
EAST BENGAL.

ORGANIZATION OF TRAUMATIC SURGERY

SIR,—I have just come across an article in the issue of the *I.M.G.* of Nov. 1944, on 'Organization of Traumatic Surgery' by Lieut.-Colonel B. K. Sheorey, I.M.S.

At the outset I must say that I fully agree with the writer in his observations, and I am sure that all surgeons in India will do the same. There is however one great obstacle to the success of the treatment, particularly in the rehabilitation in certain classes of patients.

I have had an experience as a 'surgical specialist' in the Army and now I have to deal with cases of injuries and fractures amongst workers in mills and factories—sustained during the discharge of their duties. As these patients are fully aware that the amount of compensation varies directly with the percentage of disability, they want to remain as crippled as long as possible, or at least till the compensation is decided. They will not co-operate with the surgeon in doing their best to achieve the desired result. I do not expect a solution to the problem from the writer but only wish to point out that in spite of the best organization failures will follow.

V. L. SURYAVANSHI,
Civil Surgeon.

SOLAPUR.

'DEBRIDEMENT'

SIR,—I consider that the attention of your readers should be called to the fact that a number of English-speaking surgeons are misusing the word 'debridement' with gay abandon under the misapprehension that it denotes excision and surgical revision of a wound.

I have again referred to my copy of 'Chirurgie de la Main', 'Première Partie, Chapitre Premier, Exploration Systematique', 2nd sub-para, 'Treatment de parties molles, Technique de l'excision', par Maro Iselin (Masson & Cie, 1938).

From the context it appears that M. Iselin does not consider that 'debridement' includes 'excision'. M. Iselin is a distinguished French Surgeon and should be in a position to use his own beautiful language correctly.

F. R. W. K. ALLEN.

INDIAN MILITARY HOSPITAL,
POONA,
12th March, 1945.

EFFECT OF PENICILLIN ON A CASE OF ULCUS TROPICUM (NAGA SORE)

SIR,—As I do not find in the literature any record of penicillin being used in the treatment of Naga sore, I beg to submit the following observation of mine for publication in the journal.

I used penicillin (Lilly) on a case and found very encouraging results. The patient had a well-developed typical sore on his foot measuring about $1\frac{1}{2}$ inches in diameter. Fusiform bacilli were present in the discharge in large numbers, and no other micro-organisms were seen. The following remedies had been tried in succession without satisfactory results—bathing in electrolytic chlorine followed by saline for one week, dressing with propamidine jelly (M&B) 0.1 per cent for one week, cibazol tablets per mouth, one every four hours for five doses a day as well as cibazol dusting powder on the sore once a day for four consecutive days. Pus was still copious, pain and tenderness were present and fusiform bacilli were numerous in the discharge. Then penicillin in a strength of 100 units per c.cm. was used as a wet dressing with absorbent lint and cotton, kept bandaged with oil silk so as to prevent evaporation. After one day's treatment, pus and pain were both lessened. After three days' treatment, pus was scanty, pain absent and no fusiform bacilli found. Four days' treatment showed clean granulation tissue and then penicillin was discontinued. There was no recurrence of pus and fusiform bacilli and the sore healed up within a further period of one week.

As I have no further cases of Naga sore and am unable to reproduce the sore in laboratory animals, I cannot continue my observation but I hope other workers will try the drug on the sore.

G. PANJA,
Assistant Professor of
Bacteriology.

SCHOOL OF TROPICAL MEDICINE,
CALCUTTA,
21st March, 1945.

Service Notes

APPOINTMENTS AND TRANSFERS

THE Central Government is pleased to nominate Colonel W. E. R. Dimond, C.I.E., O.B.E., Surgeon-General with the Government of Bengal, to be a member of the Medical Council of India, from Bengal, with effect from the 26th March, 1945, vice Major-General W. C. Paton, C.I.E., resigned.

To be Honorary Surgeon

Lieutenant-Colonel (T/Col.) W. E. R. Dimond, C.I.E., O.B.E., 31st October, 1944, vice Colonel W. C. Spackman, vacated.

Lieutenant-Colonel A. N. Chopra, Director of Health and Inspector-General of Prisons, Orissa, was appointed as Officer on Special Duty under the Chief Commissioner, Delhi, with effect from the 14th February, 1945.

Lieutenant-Colonel L. K. Ledger, O.B.E., Residency Surgeon, Hyderabad, on return from leave, resumed charge of his duties, with effect from the afternoon of the 24th February, 1945.

Major J. Guthrie was appointed Additional Civil Surgeon, Tibet and Bhutan, with effect from the forenoon of the 15th January, 1945.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

To be Captains

Gurdial Singh. Dated 5th February, 1944.
Het Ram Gandotra. Dated 5th February, 1944.
Jagat Singh Karanwal. Dated 16th August, 1944.
Nariman Erachshah Cooper. Dated 5th November, 1944.
Yelagalavadi Vedavyasacharya Sreenivasa Murthy. Dated 20th November, 1944.
Waman Dattatraya Sulakhe. Dated 8th December, 1944.

Homi Framji Daroga. Dated 19th December, 1944.

To be Lieutenants

Sardar Singh Dhanoa. Dated 14th October, 1944.
Kuldip Singh. Dated 21st November, 1944.
Mahendra Singh. Dated 10th December, 1944.
Promode Lal Chatterjee. Dated 24th December, 1944.

INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

(WOMEN'S BRANCH)

To be Captain

(Miss) Leela Duttatray Tilak. Dated 17th October, 1944.

The undermentioned officer of the I.M.S. has been granted Emergency Commission :—

ROYAL INDIAN AIR FORCE—MEDICAL BRANCH

To be war substantive Flight-Lieutenant

Captain Krishan Lal Chopra, 31st October, 1944 (promoted Captain 30th June, 1944).

The undermentioned officer of the I.M.S. reverts from the Indian Army Medical Corps and is seconded for service with the Royal Indian Navy :—

Major P. M. McSwiney. Dated 16th January, 1945.

The undermentioned officer of the I.M.S. reverts from the Royal Indian Navy and is seconded to the Indian Army Medical Corps :—

Major G. W. Miller. Dated 16th January, 1945.

The undermentioned officer of the I.M.S. (E.C.) reverts from Indian Army Medical Corps and is seconded for service in the Royal Indian Naval Volunteer Reserve :—

Captain K. Parthasarathy. Dated 25th January, 1945.

PROMOTIONS

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
(Emergency Commissions)
Captains to be Majors

H. M. Kalapesi. Dated 2nd January, 1945.
K. Jaswal. Dated 7th January, 1945.
15th January, 1945.
A. Dass.
S. Gnaneswaran.

D. Robertson. Dated 16th January, 1945.
 B. I. S. Bhalla. Dated 10th March, 1944.
 P. Papatla. Dated 21st June, 1944.

Lieutenants to be Captains
 3rd April, 1944

Noel Vernon Doyle.
 Arthur Rothschild Coshan.
 Denzil Ian Gantzer.
 Douglas Ashley Hugh Walton.
 Eric Meneaud Wilson.
 Michael Deryck Innis.
 Aylmer Joseph Nicholas.
 Eric Joseph Newton.
 Daniel Frederick O'Malley.
 Ivan Joseph Paul Woodhouse.
 Arthur Wright Scott Webster.
 Cyril McArthur Hogg.
 Reginald Paul Harvey.
 Clifford Owen Bedell.
 Cyril Brendon Andrade.
 Henry Arthur Garstin.
 Leslie George Raworth Hull.
 Dudley Clarence Wilkins.
 Cecil Joseph Pereira.
 Maxwell Joseph Van Ross.
 Eugene Leopold Cyril Pushong.
 Francis Walter Perreira.
 Domnius John William D'Costa.
 Clarence Joseph D'Netto.
 Basil George Bamford.
 Gerald Aloysius Burby.
 Charles Joseph Hart.
 Stanley Robert Edward Kitto.
 Arthur Donald Stanislaus McLaughlin.
 John Charles Allan Dique.
 Ernest John Goodsir Cullen.
 Joseph Michael Francis D'Mellow.
 Paul Frank D'Mellow.
 Newton Braganza.
 William Burbridge James.
 Gerald Maxwell Muller.
 Kenneth Morrison Herd.
 Meredith Carlyon Joseph Masters.
 Duncan Anthony Leonard Gibson.
 Bardley George Clarkson.
 Stephen Francis D'Costa.
 Wilfred Ian White.
 George Anthony D'Vaz.
 Joseph Anthony Righton.

15th December, 1944

D. H. Nibblett. T. A. D'Sena.
 R. M. S. Terry.

1st January, 1945

R. M. Krishnaswamy. R. Purshotaman.
 M. K. Nayak.

3rd January, 1945

P. G. Kesavalu. J. J. Barnes.
 M. E. Roby. M. A. Ramaswamy.
 K. S. Raghavan. T. A. A. Gafur.
 S. M. Ganeshiya. T. S. Kalyanam.
 S. M. Krishnan. V. R. Srinivasan.
 C. T. Simon. C. R. Aiyappan.
 K. S. Ramkrishnan. K. U. Rao.

A. B. Philip. Dated 15th January, 1944.
 P. D. Naidu. Dated 18th January, 1945.
 P. V. Rao. Dated 22nd January, 1945.
 B. Ramanarayanamurty. Dated 23rd January, 1945.
 N. N. Bhushanam. Dated 24th January, 1945.

INDIAN ARMY MEDICAL CORPS—WOMEN'S BRANCH
(Emergency Commissions)

Lieutenant to be Captain

(Miss) A. George. Dated 6th January, 1945.

RELINQUISHMENTS

Captain C. G. Bree, on grounds of ill health, 18th October, 1943.

Captain Sohan Singh Chhabra, 18th February, 1945, on grounds of ill health and is granted the honorary rank of Captain.

Captain Syed Mahmud Hussain Jafri, 24th February, 1945, on grounds of ill health and is granted the honorary rank of Captain.

Lieutenant Ramchandran Narayanan, on grounds of ill health, 8th December, 1944, and is granted the honorary rank of Lieutenant.

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Original Articles

A CLINICAL STUDY OF 89 CASES OF ENCEPHALITIS

By JYOTSNA RANJAN CHATTERJI, M.B.

Medical Registrar

N. GUPTA, M.B., M.R.C.P. (Edin.), D.T.M. & H. (Lond.),
D.P.H. (Cantab.)Professor of Clinical Medicine
and

M. N. DE, M.B., M.R.C.P. (Lond.), F.N.I.

Professor of Medicine

(From the Department of Medicine, Medical College,
Calcutta)

THE word encephalitis denotes broadly an inflammation of the brain substance characterized clinically by a febrile reaction, an unconscious or semi-conscious state, and various grades of disturbances of the function of the central nervous system. In some cases a complete recovery with restoration of the normal functions of the brain and spinal cord occurs, whilst in others severe degenerative changes take place in the brain leaving the organ permanently damaged. The condition is to be regarded as serious.

The causative factors are many, the chief of which are microbial toxins and viruses. Acute non-suppurative encephalitis of virus aetiology is not uniformly distributed all over the world, neither is its incidence very constant. It usually occurs in epidemic form, but sporadic instances may be found in places where it is least expected. While an epidemic of encephalitis was in progress in middle Europe in 1916-17, hardly any case was reported in India until 1919 when the epidemic spread to this as well as to other far eastern countries such as Japan and Eastern China. Even then, the incidence of the disease never assumed a big proportion as seen in Europe and America. That the epidemic overran our country during its global spread was proved by the presence of a fair number of men and women of our country suffering from the post-encephalitic syndrome.

During the last three years, an epidemic of encephalitis appears to have been prevalent in Calcutta as well as in the south-eastern part of Bengal. During these years, no less than 89 cases were admitted into the Medical College Hospitals under the writers, besides a fair number of cases which came into notice during routine professional work. These latter cases however are not included in the list under review owing to the difficulty of keeping them under continued observation. Out of the 89 cases observed in the hospital, 17 were admitted in 1942, 30 in 1943 and 42 in 1944. It will be seen that the incidence gradually rose and reached the peak in 1944. It is a matter of opinion whether such a steady rise in the incidence is due to the natural spread of the

epidemic amongst the susceptible community or to the unusual social, economic and hygienic conditions consequent on the war situation. It is however certain that the disease is being less frequently noticed during the last three months.

Epidemiology

Seasonal incidence.—Curve 1 (figure 1) shows that the highest incidence of the disease was in the months of September and October and the lowest in March. It was most common in the autumn when there is marked prevalence of all catarrh-producing illnesses, the catarrh of the upper respiratory tract favouring the infection. After October, there was a steady decrease, and in December, the coldest month, the incidence was comparatively low. There was a little rise in the number of admissions in the month of January after which, however, the incidence steadily fell down and reached the lowest limit in March. The summer saw another rise to a maximum in May. The rainy season showed a comparatively low incidence.

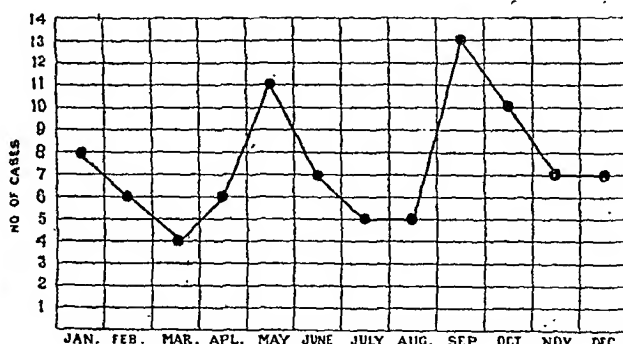


Fig. 1.

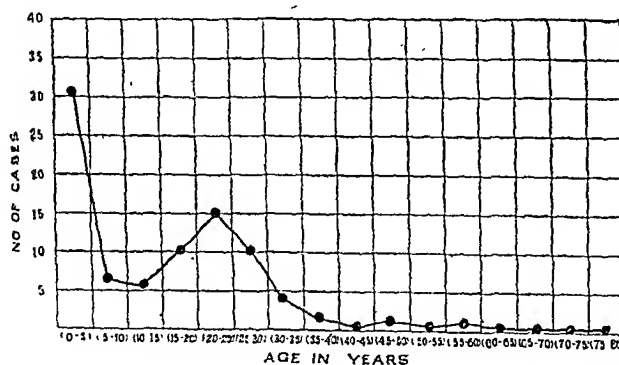


Fig. 2.

Age incidence.—It will be evident from curve 2 (figure 2) that the disease was most common in children under 5 years of age; comparatively rare between the ages of 5 and 15 years, and fairly high between 15 and 30 years. Whereas the maximum number of cases was in children under 5 years of age, the disease was rare after the age of 35 years. This may probably be explained by the lack of immunity in young children.

Sex incidence

		Adult	Child	Total
Male	..	39	17	56
Female	..	12	21	33
		51	38	89

It will be seen from the above that among adults, males were three times more affected than females, while among children the distribution was approximately equal in both sexes.

Racial incidence.—Out of 89 cases, 68 were in Hindus, 17 Muslims, 3 Anglo-Indians and one Buddhist. These figures correspond roughly to the total figures for hospital admissions of the different races, and probably do not indicate any racial variations in susceptibility.

Social status.—Most of the cases came from middle class or poor families. This may not have much significance, as the hospital cases are derived mainly from people coming from such families. The richer section of the population would not ordinarily bring their patients to be treated in the hospital. There might have also been many cases in the mofussil who could not come up to the hospital for various reasons. From a study of our series of cases, however, we got the impression that people residing in over-crowded, ill-lighted and badly-ventilated rooms of the ground floor were more prone to the disease.

Infectivity.—In our series, no instance of case-to-case infection could be found, nor could we trace a single case of familial infection.

Clinical features

As most of the patients were admitted into the hospital in an unconscious or semi-conscious state, the history was obtained mainly from the attendants. The principal complaint was fever with disturbance of consciousness occurring very early. In children, convulsions were the chief feature.

In the majority of cases, the onset was acute, starting with fever and accompanied by chill and rigor, convulsions and disturbance of consciousness. Prodromal symptoms, *e.g.* malaise, lassitude, nausea and anorexia, were present in a few only. Upper respiratory catarrh was not present in the majority of them; at any rate it was not noticed at the time of admission.

Pyrexia.—Except 4 patients who came in a collapsed condition, all had pyrexia. Continuous fever was noticed in 52 cases; in 35 less than one week's duration; and in 8 a month's duration. Intermittent fever was found in 12 cases, and remittent fever in 15. Six had irregular pyrexia of about 2 to 4 weeks' duration, and hyperpyrexia (over 106°F.) was noticed in 7 cases.

Cheyne-Stokes' breathing was noticed in 3 cases and Biot's breathing in one. Slight bronchial catarrh was noticed in a few. Tachycardia in proportion to the rise of temperature was present in the majority of them, none showing any bradycardia. A coated tongue, loss of appetite and constipation were common. Troublesome vomiting was noticed in 4 cases and slight diarrhoea in 6. Except slight albuminuria there was no abnormality in the urine.

Blood.—A moderate leucocytosis was present in 67 patients (75.27 per cent), with relative increase of polymorphonuclear neutrophil cells. Malarial parasites were not found in any one of them. Blood culture was done in 18 cases with negative results except in one which showed *D. pneumoniae*. Widal reaction for enteric group of infections was done in 23 cases, also with negative results. W.R. was negative in the few cases in which it was done.

Psychic and mental symptoms.—Disturbance of consciousness was present in almost every case. Deep unconsciousness was noticed in 57 cases and a semi-conscious state in 17. Slight somnolence or diurnal somnolence with nocturnal wakefulness was not noticed in any of our patients.

Mental symptoms were noticed in 16 patients, the symptoms varying from slight dullness to acute mania. Delirium was present in 6 cases, and was mostly violent; 2 showing delirium as found in the typhoid state. Mental confusion was noticed in 3 cases and emotional disturbances (as laughing or crying without stimulus) were present in 2.

Convulsions.—Convulsions were noticed in 38 patients of whom 27 were children under 10 years. Its incidence was maximal in infants and young children. Generalized convulsions were found in 23 cases (5 adults and 18 children) and localized convulsions in 15 (6 adults and 9 children). A past history of convulsions was given in 5 patients, 4 of whom were children under 10 years.

Meningeal irritation.—The signs of meningeal irritation such as stiffness of the muscles of the neck, a positive Kernig's sign, etc., were present in 42 cases. In some of them the meningeal irritation was so severe that without a lumbar puncture they could have easily been taken for meningitis.

Cranial nerves.—The cranial nerves having their nuclei in the mid-brain were mostly affected. A sluggish reaction to light or accommodation, and dilated, contracted or unequal pupils were noticed in 42 cases; ptosis was present in 4, in one of them it was bilateral, and squint in 3. Facial paralysis was observed in 2 cases.

Motor power.—Two patients showed hemiplegia and one monoplegia of the right lower limb. One developed spastic paraplegia with scissor gait, and a moderate degree of rigidity of the muscles was noticed in 5. One case developed flexibilitas cerea and another Parkinsonism with mask-like face and salivation. Slurring speech with marked intention tremor was seen in one case, and 2 had trismus. Bulbar symptoms, such as difficulty in swallowing, regurgitation of food and nasal voice were seen

in one case only. Torsion spasm producing wry neck was seen temporarily in one. Fine tremors in the tongue, fingers and eye-lids, specially when the latter were closed, could be detected in a few cases and they persisted for a fairly long time but ultimately disappeared completely.

Reflexes.—The tendon jerks were exaggerated in 10 patients, and in 3 of them the exaggeration was unilateral. A positive Babinski was seen in 12 cases, it being unilateral in 3. Well-developed ankle clonus was seen in 2 cases.

Sphincters.—Retention of urine was present in 8 patients. The majority of patients were constipated.

Sensory disturbance.—Sensory disturbances of the nature of hyperæsthesia, hyperalgesia and increased tenderness to pressure on the muscles were present in a few of them. Most of the patients being unconscious or semi-conscious did not respond to the sensory tests.

Cerebro-spinal fluid.—Lumbar puncture was done in 63 patients, the pressure being high in 52 and normal in 11. It was not done in the remaining cases owing to their low condition or for some other reason. The fluid in every instance was clear, and its culture yielded uniformly negative results. The proteins were increased, the sugar and chloride content remaining normal. Colloidal gold reaction was done in 4, the results being as follows—(1) 4444322000, (2) 0043222300, (3) 2111000000 and (4) 2234442000.

Prognosis

Out of the 89 patients, 64 died (71.9 per cent), the disease being more fatal in children under 5 years of age (86.8 per cent) than in adults (60.7 per cent). Those that came in deeply unconscious or with severe convulsions had invariably a bad prognosis. Hyperpyrexia was always serious and not a single patient with it survived.

Sequelæ.—Out of 25 recoveries, only 3 showed some residual signs at the time of discharge. One of them had mental symptoms, the second had ataxia, intention tremor and slight paresis of the lower limbs, and the third had facial palsy. These patients were progressing favourably but were discharged on request.

Discussion

At the beginning of the epidemic, the disease in some of the cases was mistaken for other maladies, such as acute cerebro-spinal meningitis, typhoid fever and cerebral malaria. As more and more patients came to the hospital, the clinical features became more pathognomonic and diagnosis clear. Those admitted with localized neurological findings were at once suspected to be cases of encephalitis, but quite a large proportion of them came in with pyrexia and disturbances of consciousness, the two symptoms which could be met with in a

large number of other conditions as well, especially in Calcutta. While routine clinical and laboratory investigations suggested encephalitis, the subsequent development of definite neurological signs ultimately clinched the diagnosis. The important points on which stress was laid for suspecting encephalitis were fever, disturbances of consciousness, meningeal irritation and convulsions, but with clear cerebro-spinal fluid and a moderate leucocytosis. Cerebral malaria, acute cerebro-spinal meningitis, eruptive fevers, septicæmic conditions, the enteric group of fevers and typhus fever were all considered in the differential diagnosis. The two conditions which caused the worst confusion clinically were cerebral malaria and cerebro-spinal meningitis; this was removed by a blood examination and lumbar puncture. On clinical grounds alone, this appears to be an epidemic form of encephalitis. In our series, however, we observed the following features which were different from the clinical picture of classical epidemic encephalitis.

(1) The incidence was highest in infants and young children who are least affected in epidemic encephalitis.

(2) There is a marked difference in the mortality rate between the two diseases. Whereas in epidemic encephalitis, it varies from 27 to 50 per cent, it was as high as 72 per cent in our series of cases. Moreover, most of these ran a very acute and severe course which is unusual in epidemic encephalitis.

(3) Somnolence as seen in epidemic encephalitis, *viz.* light somnolence by day with nocturnal delirium, was not found in our patients. Unconsciousness was, in the majority of them, very deep and early. Early interrupted lethargy and inversion of sleep rhythm were not detected.

(4) Convulsions were a prominent feature as opposed to its rarity in epidemic encephalitis.

(5) Meningeal irritation was also a prominent feature and the intracranial pressure as estimated by lumbar puncture was increased in most of the cases. This is different from epidemic encephalitis in which the cerebro-spinal fluid pressure is usually not raised.

(6) Localizing neurological findings were absent in many of the cases, and, when present, were rather prominent.

(7) Mortality was highest in the first week, and recovery after that period was more hopeful.

(8) Residual signs after recovery from the acute stage were infrequent.

Summary

(1) Clinical features of 89 cases of encephalitis admitted into the Medical College Hospitals under the writers during the years 1942, 1943 and 1944 are given.

(2) The differences in the clinical features observed in the present series from those of epidemic encephalitis are discussed.

The writers express their sincere gratitude to Lieut.-Colonel H. E. Murray, Superintendent, Medical College Hospitals, for his permission to carry out the work and utilize the records of the hospital.

SULPHANILYLGUANIDINE IN CHOLERA

By S. K. GUPTA, M.B., D.T.M.,
B. C. CHATTERJEE, M.B., D.T.M., D.P.H.,
B. M. PAUL, L.M.P., L.T.M.

and

R. N. GHOSE, L.M.F.

(Bowel Diseases Research Department, School of Tropical Medicine, Calcutta)

By reason of its solubility in water (200 mg. per cent according to Marshall *et al.*, 1940), and low absorbability from the gastro-intestinal tract [Marshall *et al.* (1941), Crossley *et al.* (1938)] sulphanilylguanidine remains in the intestine for a long time to act on bacteria. With this idea in view, sulphanilylguanidine was used (Chopra *et al.*, 1941) in the cholera epidemic of 1941 with good results. The mortality among the sulphanilylguanidine treated cases was 3.84 per cent whereas the death rate among the control cases treated with saline transfusions only was 8.97 per cent. The preliminary work revealed the harmless nature of the drug in cholera and we decided to administer the large doses which had lately been recommended.

While the efficacy of sulphanilylguanidine was being tried in cholera patients in the Campbell Hospital, studies were also made of its action on *V. cholerae in vitro*.

Vibrio cholerae and sulphanilylguanidine

Three tubes were taken as noted below :—

- (1) 1 gm. of sulphanilylguanidine added to 4 c.cm. of nutrient broth.
- (2) 1 gm. of sulphanilylguanidine added to 4 c.cm. of nutrient broth and autoclaved.
- (3) Sterile nutrient broth 4 c.cm.

Equal amounts of *Vibrio cholerae* were inoculated into each of the above three tubes. Thereafter cultures in bile salt agar plates were made from each of these test tubes at various intervals and the results recorded next day as stated below :—

Six tubes containing 9.9 c.cm. of nutrient broth with 0.5 per cent sulphanilylguanidine were prepared. By serial inoculation of a 20 hours' culture of cholera vibrio (Ogawa) (0.1 c.cm. of culture into tube 1, 0.1 c.cm. from tube 1 to tube 2, etc.) dilutions from $1/10^2$ to $1/10^{12}$ were prepared. Similar tubes of the same broth without sulphanilylguanidine were prepared and inoculated with cholera vibrio in the same way and in the same dilutions. The tubes were incubated for 28 hours and at the end of that time were sub-cultured on the half per cent bile salt agar plates. The results were as follows :—

Dilution of inoculum	Tubes seen after 24 hours	0.1 c.c. plated after 28 hours' action
<i>With sulphanilylguanidine (0.5 per cent)</i>		
$1/10^2$	Good growth	Heavy growth
$1/10^4$	No growth	210 colonies
$1/10^6$	"	No growth
$1/10^8$	"	"
$1/10^{10}$	"	"
$1/10^{12}$	"	"
<i>Without sulphanilylguanidine</i>		
$1/10^2$	Good growth	Many colonies
$1/10^4$	"	"
$1/10^6$	"	"
$1/10^8$	"	"
$1/10^{10}$	"	"
$1/10^{12}$	"	"

Five c.cm. were taken from each of the sulphanilylguanidine culture tubes (except the first tube) into 100 c.cm. of nutrient broth and incubated, the idea being to dilute the sulphanilylguanidine. In 24 hours there was no growth but in two of the flasks there was growth in 48 hours. The original dilution in these two cases had been 10^4 and 10^6 .

These experiments indicate the bacteriostatic and bactericidal properties of sulphanilylguanidine on the cholera vibrio.

Sulphanilylguanidine in cholera cases

The average weight of an Indian adult admitted to the cholera ward of the Campbell Hospital was roughly 50 kilograms and 5

Time of plating after addition of young culture of <i>V. cholerae</i>			Presence of <i>V. cholerae</i> or other colonies in		
			Tube 1	Tube 2	Tube 3
Immediately	Large numbers of <i>V. cholerae</i>	Large numbers of <i>V. cholerae</i>	Large numbers of <i>V. cholerae</i>
4 hours after	Do.	Do.	Do.
24 "	"	..	Fair number of <i>V. cholerae</i>	Do.	Do.
48 "	"	..	Few of <i>V. cholerae</i> and of other bacteria.	Do.	Do.
72 "	"	..	None of <i>V. cholerae</i> but large numbers of other bacteria.	Do.	Do.
96 "	"	..	Do.	Do.	Do.

TABLE I
Summary of cases of cholera (clinical) treated (A) with sulphamylguanidine, and (B) without sulphamylguanidine

Total cases	Deaths	Age in years						Duration of illness before admission to hospital in hours				Condition on admission		Number of days in hospital							Average amount of I.V. saline, pints.	Stool examination report	Stool positive up to (day)								Effect on urine secretion				
		12-20	21-30	31-40	41-50	Above 50	1-6	7-12	13-24	Above 24	Fair	Bad	Very bad	2	3	4	5	6	7 or more	1st			2nd	3rd	4th	5th	6th	7th	8th	Admitted with suppression		Passed urine in 24 hours	Passed urine in 48 hours	Passed urine in 72 hours	
A 263	3 (1.1%)	61	70	80	41	11	60	110	90	3	12	183	68	2	21	87	123	23	7	3.4	139	19	105	158	141	97	71	43	27	14	4	86	72	8	3
B 262	13 (4.96%)	59	73	83	20	18	64	106	90	2	15	197	50	.	3	42	145	56	16	5.1	136	21	106	157	148	108	94	70	30	18	8	72	23	26	23

TABLE II

Summary of bacteriologically positive cholera cases treated with sulphonylguanidine (A) and of control cases (B).

[illegible]

grammes of sulphanilylguanidine was given to the patient immediately on admission and 2.5 grammes were administered every 4 hours till 20 grammes in all were given. It took exactly 24 hours, after admission, to give the 20 grammes of sulphanilylguanidine to the cholera patients (Marshall, Bratton, Edwards and Walker used 0.1 grammes per kg. as initial dose and 0.05 gramme per kg. every 4 hours as maintenance doses in bacillary dysentery). The result was uniformly good every time. No nausea, vomiting, rash or drug fever was noticed in the series of cases treated with sulphanilylguanidine (as was found by Firor, 1940).

Two hundred and sixty-three cases of clinical cholera were treated with sulphanilylguanidine. Every alternate case received the same treatment. All cases admitted were entered in the book with a serial number. The odd numbers received the sulphanilylguanidine therapy and the even numbers received no sulphanilylguanidine treatment. Saline transfusions were given to both the groups of cases as often as necessary. Table I indicates the beneficial effect of sulphanilylguanidine in cholera.

Among the sulphanilylguanidine-treated cases, 86 were admitted with suppression of urine 72 (83.7 per cent) of which passed urine within 24 hours, and in the control group 72 cases were admitted with suppression of urine 23 (31.9 per cent) of which passed urine in 24 hours.

There were only 3 deaths among 263 cases treated with sulphanilylguanidine, the mortality rate being 1.1 per cent whereas 13 proved fatal among 262 control cases treated without sulphanilylguanidine, the death rate being 4.99 per cent.

Table II shows the superiority of sulphanilylguanidine therapy over the other methods of treatment as was done in control cases in bacteriologically-positive cholera cases.

The table shows that among the bacteriologically-positive cholera cases, the mortality rate was 1.9 per cent in a group of 158 patients treated with sulphanilylguanidine, while it was 7 per cent in the control group of 157 patients receiving no sulphanilylguanidine.

Out of the control cases developing pre-uræmic symptoms, seven were put on sulphanilylguanidine when they had little chance to recover. Everyone of them survived.

Field work.—One of us worked in the field using sulphanilylguanidine in cholera cases. No saline transfusion was given to any patient, i.e. neither the sulphanilylguanidine-treated nor the control cases received any saline injections. It was impossible to get a strictly comparable control group, but sulphanilylguanidine appeared to reduce the mortality rate.

Moreover, the recent work of Huang (1944) also supports the finding that the combined application of sulphanilylguanidine and saline injection reduces the mortality to a great extent.

Summary.—The death rate among 263 cases of cholera (diagnosed clinically) treated with sulphanilylguanidine was 1.1 per cent. The mortality among 262 cases of cholera (similar) treated without sulphanilylguanidine was 4.96 per cent. The death rate among 158 bacteriologically-positive cases of cholera treated with sulphanilylguanidine was 1.9 per cent whereas the mortality among 157 control bacteriologically-positive cases of cholera not treated with sulphanilylguanidine was 7 per cent. The difference in death rate in the control and sulphanilylguanidine treated cases is statistically significant.

The general symptoms improved much better in cases having sulphanilylguanidine than in the cases having intravenous saline alone.

None of the cases having sulphanilylguanidine developed uræmia. 83.7 per cent of cases admitted with suppression of urine passed urine within 24 hours on administration of sulphanilylguanidine.

Only 31.9 per cent of cases admitted with suppression of urine and treated with saline only (control cases) passed urine within 24 hours.

Seven control cases received sulphanilylguanidine on the development of uræmia and all recovered.

Sulphanilylguanidine has some vibriocidal and vibriostatic action *in vitro*.

The sulphanilylguanidine treated cases required less intravenous saline than the control ones. The bacteriologically-positive cases treated with sulphanilylguanidine had 4.5 pints of intravenous saline each on the average, and the bacteriologically positive control cases had 7.5 pints of the intravenous saline each.

It was also observed that the sulphanilylguanidine-treated patients passed fewer stools per day than the control ones.

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A NOTE ON THE PRESENCE OF 'O' AGGLUTININS IN THE BLOOD OF CHOLERA PATIENTS

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It is now well established that agglutinins for *V. cholera* develop in the blood of cholera patients a few days after the onset of the disease. Greig (1914) has credited two French observers, Achard and Bensaude, with having been the first to discover, in 1897, these specific agglutinins in the blood of cholera patients. Greig examined the blood of 363 persons, who had been attacked by cholera, and found that in a few cases agglutinins developed as early as the second day, although in the large majority of cases development was well marked only on the sixth day. Greig's observations were made on patients admitted to hospitals; as it was difficult to retain patients in hospitals for long periods, in only a few cases was it possible to follow the progress of the agglutinin curve further. He, however, concluded that 'so far as can be judged from the small number of examinations, a drop appears to occur in the agglutinin curve about the 20th day'. The recent study of Pasricha *et al.* (1939) also related to the period that elapses between the onset of the disease and the development of agglutinins. The maximum period for which they studied the blood of cholera patients for the presence of agglutinins was 14 days.

Previous workers have also recognized that the detection of specific agglutinins in the blood of clinically-diagnosed cholera patients throws open the possibility of retrospective diagnosis of cholera. Such a diagnosis is of special value to an epidemiologist who may be called upon to conduct a late investigation of an outbreak of cholera in any locality. On account of the belated receipt of information, it is likely that the epidemiologist may visit the affected locality only after the outbreak may have practically come to an end. Such cases frequently arise when sporadic outbreaks occur simultaneously all over the province, or when long distances and difficulties of conveyance and transmission of information make it impossible for the investigating staff to visit the localities in time. For such purposes, it is of importance to know the maximum duration over which agglutinins can be detected in appreciable strength in the blood of cholera patients. As far as we have been able to ascertain, this question of the maximum period

through which agglutinins can persist in the blood has not yet been fully investigated for different localities and under varying conditions. It is hoped that the results recorded in this paper may help workers in public health and clinical medicine in evolving a suitable method of retrospective diagnosis of cholera in localities from which belated information may be conveyed to them.

In the months of August, September and October 1944, several outbreaks of cholera were reported from different localities in Lahore district. After the termination of the epidemic, an opportunity was taken of studying the strength of agglutinins developing in the blood of persons who had previously been attacked by cholera and had survived.

Apart from Lahore city, two other localities, viz, Kasur town and Narli village in Khalra Police Station, were visited. In Lahore city, with a population of about nine lakhs, altogether 580 cholera cases resulting in 243 deaths had occurred during the period from 22nd July to 20th October, 1944. Kasur town, which is situated to the south of Lahore at a distance of about 40 miles, had its first case of cholera on 26th August, and recorded 58 cases and 29 deaths up to 5th October—the date of the last case. Narli village has a population of 3,300 and lies at a distance of 23 miles from Lahore. In this, a sharp outbreak had occurred on 18th October; it continued up to 24th October and, during these seven days, 58 persons were attacked of whom 28 died.

For the purpose of the present study, Narli village was visited on 30th January, 1945, Kasur town on 18th and 19th November, whilst blood specimens in Lahore city were collected from 1st to 17th January, 1945. The blood of the patients was collected in Wright's capsules. After separation of the clot, the serum was drawn off and dilutions of 1/25, 1/50, 1/100, 1/150, 1/200 were prepared with normal saline. An emulsion of living cholera vibrios which had previously been tested against Inaba 'O' serum and had given positive reactions showing the presence of 'O' antigen was used. The test was put up in Dreyer's agglutination tubes by using equal quantities of the emulsion and serum dilutions. Racks containing the agglutination tubes were kept in a water bath at 56°F. for two hours. Thereafter, the tubes were transferred to the refrigerator. Results were recorded on the expiry of 24 hours. The results were confirmed by the slide agglutination method in which the emulsion and the dilution of the serum were mixed on a microscopic slide. It was done on account of the ease with which the reaction of agglutination could be observed on the slide.

The results in respect of 15 specimens from the city of Lahore, 11 each from Kasur town and Narli village are summarized in the following tables. It must be mentioned that on previous bacteriological examination of stools of the clinically-diagnosed cholera patients, we had been satisfied that outbreaks of true cholera did occur in these three localities. However, we had not been able to examine bacteriologically the stools of all the recovered cases from whom specimens of blood for this study had been obtained. We made every attempt on the basis of the clinical histories and by personal enquiry to ensure that as far as possible blood specimens were obtained from only the true cases of cholera.

TABLE I

Agglutination reactions of the blood sera of recovered cholera patients in Narli village

Serial number	Dilution				
	1/25	1/50	1/100	1/150	1/200
1	—	—	—	—	—
2	—	—	—	—	—
3	—	—	—	—	—
4	+	+	—	—	—
5	+	+	+	+	—
6	+	—	—	—	—
7	+	+	+	+	—
8	+	+	+	+	—
9	—	—	—	—	—
10	+	+	+	—	—
11	—	—	—	—	—

In Narli village, out of the blood of 11 clinically diagnosed cholera patients, seven* gave

observed in three of the positive cases was 1/150.

In Kasur town, the blood of 11 patients was collected on 18th November, 1944, of which 6 specimens were positive, and in these cases the agglutinins were found to persist for about two months following the date of attack. The highest titre observed in two of the positive cases was 1/150.

As against the experience of Narli village and Kasur town, the number of positive reactions in Lahore is very low. Only one case out of the 15 examined showed the presence of agglutinins. The highest titre observed in that case was 1/100.

It may be noted that the interval between the date of blood examination and the date of attack in Lahore was in some cases nearly four months, and this long period may be a possible explanation for the small number of positives.

TABLE II

Agglutination reactions of the blood sera of recovered cholera patients in Kasur town

Serial number	Dilution					Date of attack	Days elapsing between dates of attack and blood examination
	1/25	1/50	1/100	1/150	1/200		
1	+	+	+	—	—	19-9-44	60
2	+	+	+	+	—	19-9-44	60
3	—	—	—	—	—	16-9-44	63
4	+	+	—	—	—	19-9-44	60
5	+	+	—	+	—	15-9-44	64
6	+	+	+	+	—	15-9-44	64
7	+	+	—	—	—	19-9-44	60
8	—	—	—	—	—	15-9-44	64
9	—	—	—	—	—	11-9-44	68
10	—	—	—	—	—	7-9-44	72
11	—	—	—	—	—	12-9-44	67

TABLE III

Agglutination reactions of the blood sera of recovered cholera patients in Lahore city

Serial number	Dilution					Date of attack	Date on which blood sample was taken	Days elapsing between dates of attack and blood examination
	1/25	1/50	1/100	1/150	1/200			
1	—	—	—	—	—	26-8-44	1-12-44	97
2	—	—	—	—	—	26-8-44	1-12-44	97
3	—	—	—	—	—	26-8-44	1-12-44	97
4	—	—	—	—	—	16-8-44	4-12-44	110
5	—	—	—	—	—	27-8-44	4-12-44	99
6	—	—	—	—	—	27-8-44	4-12-44	99
7	—	—	—	—	—	27-8-44	4-12-44	99
8	—	—	—	—	—	26-8-44	4-12-44	100
9	—	—	—	—	—	26-8-44	17-1-45	113
10	—	—	—	—	—	26-8-44	17-1-45	113
11	—	—	—	—	—	26-8-44	17-1-45	113
12	—	—	—	—	—	26-8-44	17-1-45	113
13	—	—	—	—	—	29-8-44	17-1-45	110
14	+	+	+	—	—	26-8-44	17-1-45	113
15	—	—	—	—	—	26-8-44	17-1-45	113

positive results. Thus, as high a percentage as 64 of positive reactions has been observed even after a lapse of 102 days from the date of attack (20th October, 1944). The highest titre

Summary and conclusions.—With a view to studying the length of the period over which agglutinins for cholera may persist in patients, blood examinations of recovered cholera patients were carried out in three different localities,

* Table I shows only six positives.—Editor.

riz, Lahore city, Kasur town and Narli village in Lahore district. The study indicates that agglutinins can persist in the blood of recovered cases of cholera up to a period of three and a half months and possibly more. For epidemiological purposes this finding can be utilized for a retrospective diagnosis of an outbreak of cholera if, for unavoidable reasons, an opportunity for the bacteriological examination of stools has been missed during the course of the outbreak.

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SULPHANILYL BENZAMIDE IN THE TREATMENT OF BACILLARY DYSENTERY*

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TREATMENT of bacillary dysentery with sulphaguanidine, succinyl sulphathiazole and other sulpha drugs has opened a new line of investigation (Marshall *et al.*, 1940). Many papers have already been published reporting the clinical efficacy of sulphaguanidine, but this drug has certain drawbacks due to toxic effects. Sometimes it causes vomiting and thus its use is often precluded in cases which need it most (Hughes, 1944). Symptoms such as rashes, nausea, headache, tachycardia and fever are not uncommon (Smith, 1944; Brewer, 1943). The dosage used is usually large—an adult of average weight requiring a total dose of at least 100 to 116 tablets of 0.5 gramme each (Clay, 1943). Moreover, sulphaguanidine is not effective against *Bacillus dysentery* Sonne (Fairbrother, 1944). Bose and Ghosh (1944), during their study on sulphanilyl benzamide prepared in this laboratory, found that this compound is of very low toxicity. Mice tolerate a dose of 1 mg./gm. intraperitoneally and intravenously without any mortality. Further, it was observed that a concentration of 1:10,000 inhibited the growth of *Bacillus dysentery* Flexner whereas sulphaguanidine inhibits in 1:5,000 only (cf. Brownlee and Tonkin, 1941).

In view of its low toxicity as well as its high bacteriostatic activity against Flexner organism, it was considered worth while to study its effect on clinical cases of bacillary dysentery. During the months of July and August last year, there came an opportunity of treating 21 bacillary dysentery patients all of whom were workers of this laboratory.

Clinical features.—All patients were adult males between 20 and 40 years of age. Pyrexia

was not a prominent feature, and, when present, it usually subsided within 48 hours of beginning the treatment. Immediately after admission, the frequency and character of the stools were noted and specimens taken to the laboratory for plating and microscopical examination. The cases were on the whole of a mild type with not more than 8 to 10 stools a day. The clinical appearance of the stools varied between loose offensive motions and the pus-blood-mucus dysentery stools. The typical bacillary dysentery picture was seen under the microscope, e.g. plenty of pus cells, red cells, macrophage cells and very few bacteria. On culture, the following results were obtained:—

S. dysenteriae (Shiga) 2, *S. paradysenteriae* (Flexner) 10, *S. paradysenteriae* (Hiss) 2, *Bacillus asiaticus* 1 and *Bacillus pseudo-carolinus* 1.

In 5 cases, no dysentery organisms could be isolated, but the clinical symptoms and microscopical findings were suggestive of bacillary dysentery.

Treatment.—On the first two days, 6 tablets of sulphanilyl benzamide (0.5 gm. each) were given in three divided doses at 4-hourly intervals. During the next four days, 4 tablets were given daily in 4 doses at 4-hourly intervals. This six days' treatment was quite sufficient to bring about a complete cure in almost all cases except the two cases infected with *B. dysentery* Shiga which required the treatment for a little longer period for their cure. A total dose of 14 grammes (28 tablets) was necessary for one patient. Nothing else was given except sodium bicarbonate ten grains along with each dose of tablets and also glucose.

Results

Within 24 hours of commencing treatment, improvement started. The number of stools came down to 2 or 3, blood and mucus disappeared within 36 hours, and formed stools were passed on the third day. On the fifth day the patients resumed work. After clinical cure, the stool from each case was cultured once a week for three months with negative results. No relapse has occurred in any of the cases within the six months of observation period. No toxic manifestations such as nausea, vomiting, headache, rashes, tachycardia, etc., were encountered in any of the cases. The result of treatment shows that the compound sulphanilyl benzamide is an effective chemotherapeutic agent against bacillary dysentery (Swyer and Yang, 1945).

Summary

Twenty-one cases of bacillary dysentery were treated with sulphanilyl benzamide; 16 were bacteriologically positive.

The total dose required was only 14 grammes (28 tablets) for complete cure except in two cases with Shiga infection which required a little longer treatment. Almost all the patients were fit to resume work within five days. Stool culture was done up to three

* This paper and this subject are discussed in an editorial in our next number.—Editor.

months with negative results in all cases. No relapse was seen up to a period of six months' observation. The drug is found to be non-toxic.

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THE ACTION OF DRUGS ON DYSENTERY BACTERIOPHAGE*

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QUESTIONS are often asked by practitioners whether dysentery bacteriophage and chemotherapeutic drugs could be given simultaneously and whether the action of phage is hindered by these drugs. The following experiments were undertaken in answer to such questions.

First experiment

A strong dysentery phage was diluted by mixing 1 drop with 20 c.cm. of broth and from this

*The paper was read before the Indian Science Congress Association held at Nagpur in January 1945.

mixture 5 drops were added to 100 c.cm. of broth. A small quantity from this final dilution was mixed with an equal quantity of young broth culture of *Bact. flexneri* and plated on pepsin agar medium. Discrete phage plaques were seen after 18 to 20 hours' incubation. The above diluted phage as well as strong phage were used for the experiments. Solutions and suspensions of the drugs were made in distilled water and kept in contact with equal quantities of phage at room temperature for one to two hours and then filtered through L₃ candles. The filtrates were tested for the presence of phage, and the results are given in table I.

Phage could be recovered from the area of lysis. Distinct plaques indicated that lysis was due to phage action and not due to the bactericidal action of the drugs, as bacteria were found not killed by the drugs outside the plaques.

It will be seen that the above three chemotherapeutic drugs in 1 per cent strength, phenol 0.5 per cent and electrolytic chlorine 0.25 per cent do not inactivate dysentery phage in 1 to 2 hours *in vitro*. Phage boiled for 2 minutes is inactivated.

Second experiment

This was done with double the concentrations of solutions and suspensions, and an increase in the time of contact. For results see table II.

It will be seen that 2 per cent strengths of the above chemotherapeutic drugs and phenol 1 per cent do not inactivate the dysentery phage in 2 to 3 hours *in vitro*. Electrolytic chlorine 0.25 per cent partially inactivates it in 3 hours. Boiling for 5 minutes kills the phage. Clear areas are due to lysis of bacteria, as the drugs alone do not give rise to such clear areas.

TABLE I
 Growth of dysentery phage in solutions of the sulpha drugs, etc.

Drugs	M.&B. 693	Sulpha-guanidine	Solu-septasine	Phenol	Electrolytic chlorine	Phage boiled for 2 minutes	Control, i.e. phage without any treatment
Percentage ..	1	1	1	0.5	0.25
Time of contact, hours	1	1	2	2	2	0	0
A loopful of filtrate touched on culture of dysentery bacilli spread on solid medium.	L	L	L	L	L	—	L
A loopful mixed with 3 to 4 loopfuls of culture and spread.	+	++	+	+	+	—	+
1 to 2 c.cm. of filtrate mixed with 10 to 15 drops of culture and spread.	++	++	+	+	+	—	+++

L = complete lysis; + = plaques present; — = no plaques, no lysis.

TABLE II

Growth of dysentery phage in solutions of the sulpha drugs, etc., in increased concentrations and time of contact

Drugs	M.&B. 693	Sulpha-guanidine	Solu-septasine	Phenol	Electrolytic chlorine	Phage boiled for 5 minutes	Control without boiling
Percentage ..	2	2	2	1	0.5
Time of contact, hours	2	2	3	3	3	2	—
A loopful of filtrate touched on spread culture of dysentery bacilli.	L	L	L	L	(L)	—	L
One loopful of filtrate mixed with one loopful of culture and spread.	+++	+++	++++	+++	++	—	+++
Equal amounts of filtrate mixed with equal amounts of culture in liquid medium.	L	L	L	L	(L)	—	L
A loopful of drug alone touched on spread culture.	—	—	—	(+)	(+)

(+)= Partial clearing. (L)= incomplete lysis.

TABLE III

Growth of undiluted dysentery phage in solutions of the sulpha drugs, etc., in increased concentrations and time of contact

Drugs	M.&B. 693	Sulpha-guanidine	Solu-septasine	Phenol	Electrolytic chlorine	Boiled for 5 minutes	Control
Percentage ..	2	2	2	1	0.5
Time of contact, hours	2	2	24	24	24	4	4
One loopful of filtrate touched on spread culture of dysentery bacilli.	L	L	L	L	L	(L)	L
One drop of filtrate mixed with 5 to 6 c.c. of broth culture and spread.	+ ⁿ	+ ⁿ	+ ⁿ	+ ⁿ	+ ⁿ	(+)	+ ⁿ

+ⁿ = confluent phage plaques and no bacterial growth; (L) = incomplete lysis; (+) = a few phage colonies are present.

Third experiment with undiluted strong phage

One drop of strong phage is added to the drugs. The time of contact and concentrations are as in table III.

Conclusion

Two per cent strengths of the above chemotherapeutic drugs, phenol 1 per cent and

electrolytic chlorine 0.5 per cent have no action on strong dysentery phage. Boiling of a strong phage for 5 minutes does not completely kill it.

It was not considered necessary to carry on the experiments further, as in practice, the above chemotherapeutic drugs and the bacteriophage do not reach such a high concentration in the gut.

SCABIES IN BENGAL

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In recent years, many reports have appeared alleging that scabies was epidemic in Bengal and other parts of India and that the disease was affecting a high proportion of the population. There was, however, some doubt as to whether all the so-called 'scabies' was in fact due to *Sarcoptes*, or whether some of the skin conditions noted were not due primarily to malnutrition and actual famine.

Knowing that I was likely to be in Calcutta, I discussed this matter with the public health authorities with the Government of India, who expressed the hope that, if at all possible, I would attempt to investigate this question while in Bengal and try to estimate whether it was indeed true scabies. I also discussed with them new prophylactic and curative methods which might possibly be applicable to Indian conditions.

While looking into this matter in Calcutta, I received much assistance from the Director, from Dr. Lowe and staff of the Calcutta School of Tropical Medicine, Dr. Grant of the All-India Institute of Hygiene and Public Health, the Director of Public Health, Bengal, and his assistants, and was also able to discuss with several members of the Friends Ambulance Unit, who have been engaged in relief work in the areas in Bengal affected by the famine. It is due to the co-operation of these various authorities that I was able to examine patients with skin infections at the out-patients' clinic at the school, among in-patients in the hospital and in a camp for destitutes. The following conclusions were reached as a result of these examinations and discussions:—

(1) The majority of patients are suffering from true scabies, *i.e.* from infection with *Sarcoptes scabiei*.

(2) This condition is widespread. The majority of destitutes show signs of present or recent infection, and a similar state probably exists in a wide section of the population.

(3) Although *Sarcoptes* is the causative organism, it is difficult to find live mites. This is because they are present in very scanty numbers, not because they are difficult to find in pigmented skin (where present they are easily recognized).

(4) Most patients have been infected for years, and have developed a substantial immunity to *Sarcoptes*, hence the small numbers of parasites. But due to the widespread existence of the disease, over-crowding, and the warm moist climate (resembling a permanent 'in bed' microclimate) re-infection constantly occurs, and these hypersensitive individuals give a maximum reaction.

(5) I saw no individuals who had developed any tolerance to *Sarcoptes*.

(6) The widespread skin lesions are almost entirely secondary to the scabies. It is possible

that malnutrition plays a part here. Some dermatitis is due to over-treatment with sulphur (usually accompanied by active scabies in healthy, untreated skin on other parts of the body).

(7) When the scabies is cured, and re-infection prevented, the secondary lesions can be cured also.

Future action

It would be impracticable to try to set up clinics as in Britain to treat all cases and their families. The problem is a vast one, made even greater by difficulties due to caste and social custom.

In a previous communication (Mellanby, 1945) the author referred to a soap, known as 'tetmosol' soap, that has been produced for the treatment of scabies. If we could insure that all concerned used it, the disease would soon be eliminated. At present, however, poverty prevents the widespread use of any kind of soap.

In India, people not only wash but also rub oil into the skin, covering the entire surface of the body daily. If this oil could be suitably modified it might be used to eliminate scabies. A small percentage of tetmosol might be incorporated in oil used for washing purposes, or perhaps one or two per cent of 'mitigal'.

In my view, since the people of this country are so familiar with rubbing oil on the skin, it would be best, if possible, to try to incorporate any scabies remedy in this medium.

Readers of this article will, probably, be interested to learn that I have referred the matter to the Public Health Commissioner with the Government of India and also to my authorities, the Medical Research Council in the United Kingdom. I would express the tentative view that it is probable that, here in India, the end of the scabies epidemic is approaching on account of the rise in immune population resulting from the widespread outbreak, but it must be remembered that if the disease slowly decreases in extent, a non-immune population will again arise. In any event, efforts made at the present stage to control the incidence of scabies will greatly accelerate the natural decrease in the number of victims.

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NON-TRAUMATIC RUPTURE OF SPLEEN WITH A CASE REPORT

By S. C. GUPTA

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NON-TRAUMATIC or spontaneous rupture of the spleen is not rare in this country where pathological condition of the organ is so frequent.

The diseases of the spleen that predispose to its rupture are:—

1. Diseases of the spleen proper, *e.g.* infarction, torsion of the pedicle, tuberculosis of the spleen, hydatid cyst, abscess, etc.

2. Systemic illnesses that cause enlargement of the spleen :

- (a) Tropical diseases, *e.g.* malaria, kala-azar.
- (b) Infectious diseases, *e.g.* typhoid fever, influenza.
- (c) Toxæmia and pyæmic conditions, *e.g.* cellulitis, carbuncle.

In the above pathological conditions the changes in the spleen are :—

1. Replacement of the supporting framework of unstriated muscular tissue and elastic connective tissue by fibrous tissue and rigidity of the walls of the blood vessels.

2. Congestion of the pulp giving rise to increased tension under the capsule and softening of the texture.

A non-traumatic rupture is usually the combined result of the pathological changes. First sub-capsular hæmatoma results; later on the weakened capsule also yields leading to escape of blood into the peritoneal cavity. Cases are met with where laparotomy for acute pain in the abdomen revealed sub-capsular hæmatoma and not actual rupture.

Clinical features of non-traumatic rupture resemble those of perforation of a hollow viscus.

A more or less normal individual suddenly complains of pain in the abdomen which is also referred to the tip of the left shoulder (Kehr's sign) with collapse, vomiting and intestinal paresis. There is, in addition, abdominal rigidity, tenderness and shifting dullness in the flanks. But this dullness may not shift in the left side from the presence of clotted blood in that region (Ballance's sign). Soft friction sounds may in some cases be audible in the left hypochondriac region (Villibo's sign).

The following case was recently seen :—

M. T., 30 years, was admitted into the Burdwan Fraser Hospital on 9th June, 1944, at 11 p.m. for pain in the abdomen, nausea, and constipation since 9 a.m.

The patient, an inhabitant of Rawalpindi district, was employed at Panagarh in the district of Burdwan (a highly malarious place where the spleen index is 90 per cent) for a little over two months. He said that about 2 weeks after his arrival at Panagarh he had fever with rigor for about a week for which he was treated by his medical officer.

On the morning of 9th June, 1944, his bowels did not move satisfactorily and at about 9 a.m. when he was reading his holy book in a sitting posture, he felt sick and a severe pain in the left iliac region. He himself walked to his medical officer who gave him a dose of magnesium sulphate, but his pain gradually increased involving the whole of the lower abdomen and was referred to his left shoulder. A soap and water enema was also given with no result.

Condition on admission.—Pulse 80 per minute, volume and tension—fair; respiration—24 per minute; temperature—98.4°F.; tongue—clean and moist.

The patient was in great distress and pointed to his left iliac fossa and shoulder as the most painful areas. The abdomen was moderately distended. Mobility with respiration was restricted in the umbilical, left lumbar, hypochondriac and hypogastric regions; muscle guard ++ in the left lumbar and in the iliac regions. Tenderness +++ over 2 inches to the left of the umbilicus. Shifting dullness ++. Liver dullness unobliterated. Two repeated high enemas produced no result. A pre-operative diagnosis of 'perforative peritonitis' was made. The stomach was washed out.

Operation.—Under chloroform-ether anaesthesia, the abdomen was opened with a medial sub-umbilical

incision. Dark red blood welled out from the opening. Exploration revealed the presence of blood clots in the left hypochondriac region. A diagnosis of rupture of the spleen was therefore made, and the incision was enlarged up to the ensiform cartilage. As this did not give adequate exposure, the left rectus was divided across about an inch above the umbilicus. The spleen was delivered. The rupture was found on its visceral surface; its pedicle was tied with interlocked stitches in compartment from the posterior aspect. The organ was removed, the abdomen was emptied of blood as far as possible and the wall was closed in layers.

The removed spleen showed a ragged rupture 2½ inches on its renal surface at the level with the lower part of hilum. It was 5½ inches long and weighed over 9 ounces.

The patient's blood was examined after the operation, which showed no malaria parasite. After a stormy convalescence and delayed wound suppuration, the patient was discharged cured on 29th July, 1944.

In this case, there was absolutely no history of trauma. The patient developed symptoms when he was practically at rest. The case is thus an example of true non-traumatic or spontaneous rupture of the spleen. The fever with rigor, a few weeks prior to the rupture, was probably malarial. The spleen was enlarged and therefore pathological.

I am thankful to Captain J. P. Dutt, Superintendent, Burdwan Fraser Hospital, for kindly permitting me to report this case.

CONGENITAL ABSENCE OF THE SHAFT OF THE FEMUR ON BOTH SIDES

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Introduction.—Congenital absence of the shaft of the femur is very rarely described in the medical literature. The commonest congenital abnormality mentioned up till now consists of deformity or defective and retarded growth, or defective ossification, of the upper half of the shaft of the femur. The radiographs in these cases reveal that the upper half of the femur is absent. But subsequent operative procedures in these cases have shown that actually there is a cartilaginous portion present, representing the upper half of the shaft of the femur. At later ages, from 20 to 25, the radiographs of such cases show evidence of partial ossification in the cartilaginous portion of the femur.

Development and ossification.—Under normal circumstances the femur is developed mainly from five ossifying centres. The nucleus for the shaft of the femur appears at the 7th week of foetal life; the nucleus for the epiphysis of the lower end appears at birth; the nucleus for the head appears at about 10 to 12 months; the greater trochanter is ossified from one or more nuclei, which appear about the 4th year; the nucleus for the lesser trochanter appears about the 8th to 10th year.

The fusion of the epiphysis with the diaphysis is generally complete by the age of 18 to 20 years. This complete ossification of the femur is sometimes retarded due to defects in development and growth.

Case.—Rameswar, male, aged 30-32 years, resident of Assam (Nunmati), height 3 feet 6 inches, height from toes to umbilicus 1 foot 10 inches, from umbilicus to vertex 1 foot 8 inches, weight 78 lb.; while seen walking looks a sort of a Lilliputian being, with a peculiar waddling gait, rather characteristic of achondroplasia, the fingers of the hand almost reaching up to the ground (figure 1, plate X). He is a well-nourished individual who has been working as a labourer for nearly two years, or more, without much discomfort, except in locomotion, and can walk without exhaustion a distance of 2 to 3 miles. The family history is of no importance.

Physical examination.—The first and the most characteristic thing noticed is absence of the thigh on both sides. The knee joint is situated just next to the pelvis, in the usual place for the hip joint. Both sides are symmetrical; the fusion of the knee with the trunk presents an irregular boggy muscular swelling, of the size of a large coconut. The inferior extremity below the knee joint is quite normal. The portion of the trunk from the pelvis upwards is normal. The left hand is a typical claw-hand, having three fingers. No other abnormality is noticed. The movements at both knee joints are normal, the flexion being restricted to some extent. In addition to the normal flexion and extension movements at the knee, there appears to be a circumduction movement present, which is normally present at the hip. Actually the movement of circumduction is not in the knee joint, but appears to be such due to the physical deformity. This movement of circumduction takes place between the comparatively well-formed condyles of the femur, which are concave proximally, and the under-developed head of the femur, together with the anterior and inferior portion of the ischium, resting partially on the condyles. There is possibly a false joint formed here. It is at this place that this circumduction movement occurs. The body weight seems to be transferred through this portion of the ischium and the head of the femur resting on the concavity of the condyles. Another feature noticed is the absence of normal patellæ on both sides.

X-ray findings.—**Pelvis.** The A. P. view shows absence of femoral shafts on both sides. The femoral heads are small, forming only rudimentary hip joints. It appears more likely that they are fused with the pelvis. The acetabula are shallower and wider than normal. The inferior condyles are fairly well formed with a concavity at the proximal end. They appear rotated on the vertical axis. The patellæ on both sides are represented by small streaks of osseous tissue. The knee joints except for the patellæ, are normal (figure 3, plate X).

Left hand.—A radiograph presents a typical claw-hand with two metacarpals, three phalanges, and fusion of the carpal bones (figure 2, plate X).

Conclusion.—This is probably a unique case of congenital bilateral absence of the femoral shafts. The age of the patient suggests that, if a cartilaginous rudimentary shaft was present, it would show some signs of ossification by this age. The only way to confirm this is by an operative procedure or by introducing air into the joint and subsequent x-ray. For either of these examinations the patient is unfortunately unwilling.

ATYPICAL MALARIAL GAMETOCYTES IN THE PERIPHERAL BLOOD*

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IN January 1941, a woman in her seventh month of pregnancy was referred to me for investigation by the civil surgeon and was admitted to hospital in a state of collapse. Blood smears showed a very heavy malarial infection, predominantly malignant tertian, some corpuscles showing as many as eight rings. A few rings corresponding to those of the quartan parasite and a few sporulating bodies with fully formed eight spores were present without any quartan gametocytes, suggesting that the quartan infection was a recent one. On the other hand, the malignant tertian parasite was present in all stages of development, but the classical crescent was conspicuous by its absence (see photo-micrographs on the plate).

Figure 1 (plate XI) shows a male gametocyte which looks to be the most highly developed. It is an oval body without any vestige of the containing corpuscle. Figure 2 (plate XI) shows the advanced female form. The female forms are (a) elongated and narrow, (b) spindle shaped with blunt ends, and (c) less tapering than normal towards the ends, which are blunt. None of these appear to correspond to any figures of Thomson (1912) or Brumpt (1927). In the absence of the usual crescents, these observations appear to indicate one of the following three possibilities: (i) that these forms represent the pre-crescentic stage of the gametocytes of *Plasmodium falciparum*, (ii) that they are variants of the mature crescents which in severe infections may show a change in morphology, (iii) that they might represent the gametocytes of a new parasite. This is most unlikely.

Recently a slide was sent to me by a practitioner for examination in which the above forms along with other developmental forms and without typical crescents were present.

SULPHANILAMIDE IN ACUTE NEPHRITIS

A STUDY OF 22 CASES

By S. T. ACHAR, M.D.

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THE close relation of acute nephritis to infections with the hæmolytic streptococcus has been recognized for many years, and it is therefore tempting to suppose that drugs of the

*[The case appears to show stages of developing gametocytes of *P. falciparum* in the peripheral blood. Das Gupta and Ganguly reported a similar case in the October 1944 issue of the *Gazette*.—Editor, I.M.G.J.]



Fig. 1.—Photograph of the patient.
 Standing. Height—3 feet 6 inches.



Fig. 2.—Radiograph of left hand.

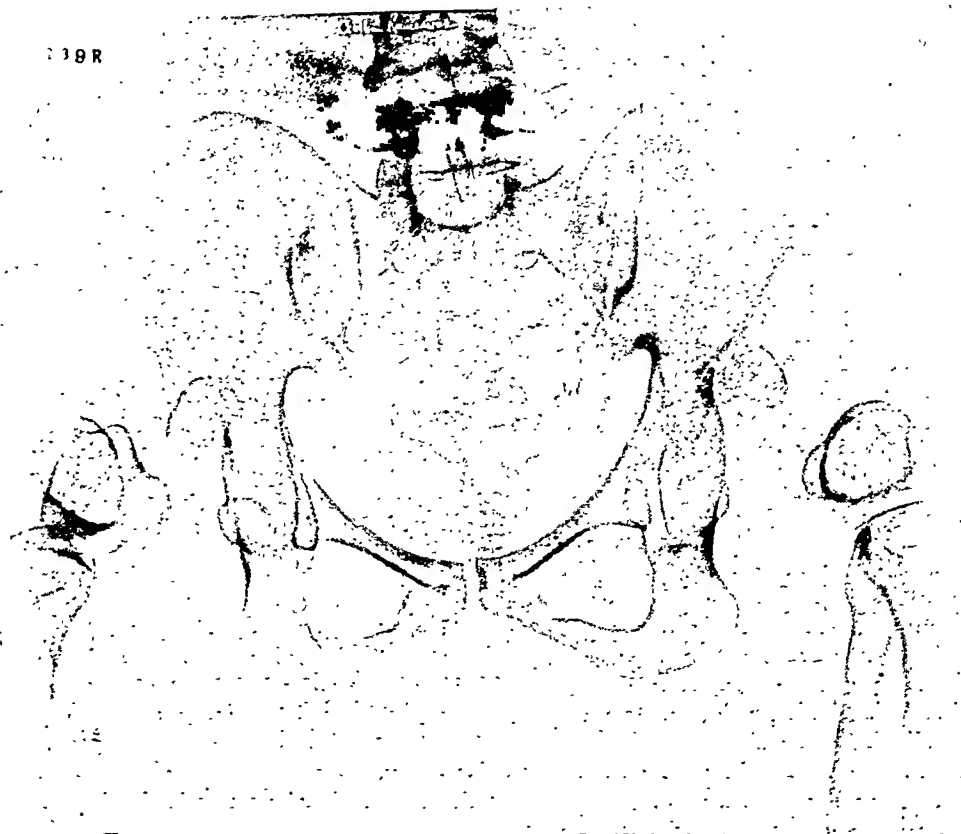


Fig. 3.—A.P. view of pelvis.

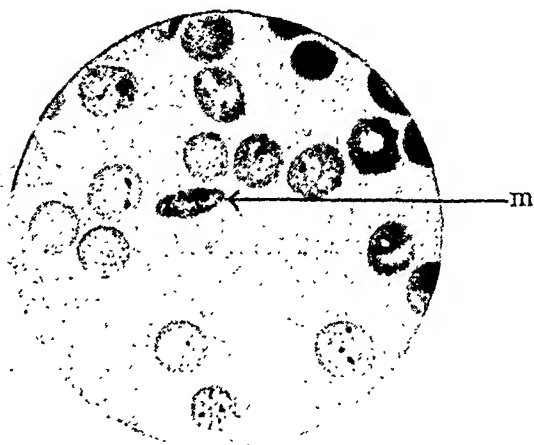


Fig. 1.—m = A male gametocyte.

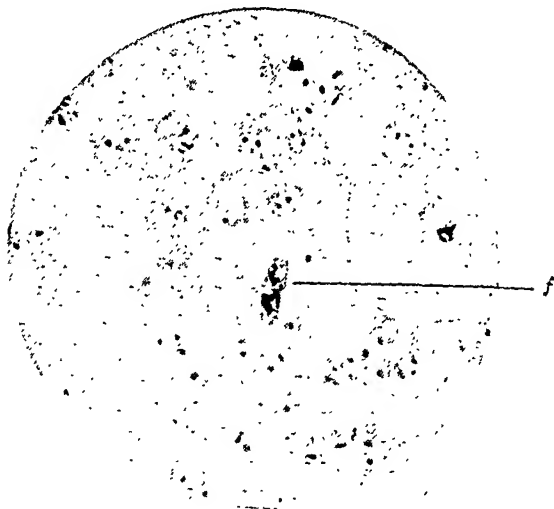


Fig. 2.—f = A female gametocyte.

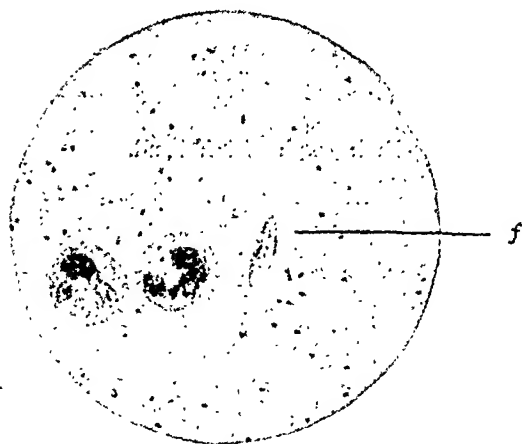


Fig. 3.—f = A female gametocyte with both ends pointed.

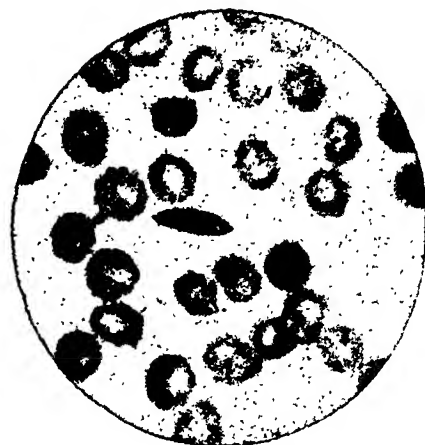


Fig. 4.—Another example of a female gametocyte in spindle stage.



Fig. 5.—d = A developing male gametocyte occupying half the red cell.

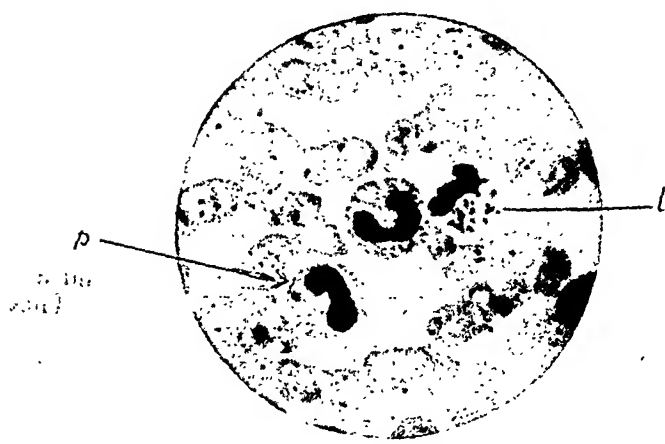


Fig. 6.—Neutrophils phagocytosing
 l = spores.
 p = pigment.

sulphonamide series might have a beneficial action on the course of the nephritic process. While sulphonamides in every form have been tried and reported upon extensively in a variety of coccal, bacterial, and even virus diseases, there has been a reluctance among physicians to exhibit this drug in acute nephritis, in spite of its accredited streptococcal origin. Probably this reluctance is traceable to the all too familiar urinary toxic complication associated with sulphonamide therapy; but when it is remembered that this anuria is considered to be a mechanical process of deposition of the insoluble acetyl derivative in the urinary tract, and that the sulpha drugs do not appear to affect the renal elements injuriously, much of the fear seems unfounded. There is however on theoretical grounds increased risk of deposition of crystals in acute nephritis, because of the inability of the inflamed kidney to excrete water readily and so flush out any minute crystals that might have formed. The hæmaturia that occurs before anuria during sulphonamide therapy is the result of hæmorrhagic pyelitis and ureteritis consequent on the mechanical irritation of the crystals, while the hæmaturia of acute nephritis has its origin in the glomeruli and has a different ætiological significance. So the constant presence of macroscopic or microscopic blood in acute nephritis cannot be advanced as an argument against the use of the sulpha drugs. The earlier reports on sulpha drugs and nephritis were based on stray cases and were inconclusive. Some (Scherber, 1935; Tixier and Eck, 1935; Slatineanu *et al.*, 1936) have noted the clearing up of nephritic symptoms in streptococcal infections, while Colebrook and Kenny (1936) have recorded the appearance of albumin, red cells and casts in the urine in cases of puerperal sepsis under prontosil therapy. Schwenker *et al.* (1937) observed the appearance of acute nephritis in a case of streptococcal meningitis under sulphonamide therapy, which disappeared on stopping sulphonamides. Williams, Longcope and Janeway (1942) have however reported very favourably on the use of this drug in a series of 42 cases.

The present investigations were started in the middle of 1943, in a series of 22 cases of acute glomerular nephritis, comprising 16 in the Government General Hospital, Madras, and 6 in the King George Hospital, Vizagapatam. They were treated with sulphanilamide, and form the subject of this paper and the end results are compared with 19 control cases treated without sulphanilamide. The prevalence in epidemic form of scabies in Madras during the latter half of 1943 and early 1944 with attendant coccal dermatitis brought in its trail an increased incidence of acute nephritis. A large proportion of the cases in this series belong to this group. All the cases on admission had varying degrees of œdema, albuminuria, and cylindruria, the presence of generalized œdema

serving to emphasize the diagnosis as glomerular nephritis as opposed to focal nephritis, though it is being increasingly recognized now that focal nephritis is but a mild variant of acute glomerular nephritis (Payne and Illingworth, 1940; Hadfield and Garrod, 1942). In the majority of these cases (15 out of 22) there were associated skin lesions (impetiginized scabies or impetigo) while in 3 there was a recent history of scabies with scars on the skin. In the remaining 4, there were no skin lesions and no history of scabies, but the tonsils were definitely unhealthy in 3, while in one, there was a history of frequent attacks of cold, and hæmolytic streptococci were cultured from throat swabs. All of them were treated with sulphanilamide orally and no remedies were applied to the skin.

Tables I to VII show the relevant clinical features in these 22 cases.

TABLE I
Age incidence

Age	Number of cases
6-12 years ..	7
12-25 " ..	8
25-30 " ..	7

TABLE II
Ætiological factors

Probable source of infection	Number of cases
Tonsils ..	3
Throat other than tonsils ..	1
Scabies without much impetiginization ..	5
Scabies with impetiginization ..	5
Marks of recently healed scabies ..	3
Impetigo ..	5

TABLE III
Duration of skin lesions before onset of nephritis

Duration	Number of cases
4-6 weeks ..	8
8-10 " ..	4
Over 3 " months ..	6

TABLE IV
Duration of œdema before admission into hospital

Duration	Number of cases
1 week and less ..	10
1-2 weeks ..	8
2-3 " ..	2
3-6 " ..	1
Chronic (6 months) ..	1

The urine was cultured in 16 of the above series, with negative results. Leaving aside one case of chronic nephritis with acute exacerbation, in which sulphanilamide controlled the

TABLE V
Urine analysis on admission

Frank hæmaturia	Smoky urine	Albumin ++	Albumin +++	Microscopic red cells and casts	Culture
1	12	7	15	All cases	Negative in the 16 cases in which it was done.

TABLE VI
Blood pressure on admission

Markedly raised	Slightly raised	Normal
5	12	5

TABLE VII
Total amount of sulphanilamide used

Amount of sulphanilamide. (gms.)	19-22	12-16	8-11	Less than 8
Number of cases.	2	14	4	2*

* More sulphanilamide could not be given to these 2 cases as they died of uræmia within 3 days of admission.

The control series of 19 cases were from another unit of the hospital during the same period (1943-44) with nearly the same proportion in the ætiological factors. Treatment adopted in the control series was on the usual standard lines, rest, diet, alkaline diuretics, mild purgatives and treatment for scabies and impetigo when present by external remedies. It will be seen by comparison that there was a much greater percentage of definite cures and fewer cases that left hospital with albuminuria in the first series table VIII. The time taken for the cure was also much shorter (table IX).

Six of the cured cases from the first series presented themselves from time to time for re-examination, and they had no recurrence of symptoms or albuminuria. In most of the cases with impetiginization, the skin condition also improved. Sulphanilamide was used in preference to sulphathiazole or sulphapyridine, as it was thought that there was less likelihood of the formation of the insoluble acetyl compound with sulphanilamide; also sulphanilamide was preferred to other sulpha compounds in hæmolytic streptococcal infections. The routine adopted in an adult was 2 pills (1 gramme) statim and one four-hourly for 5 to 7 days. In no case was the drug exhibited for more than 8 days. Children were given a proportionate dosage. The two patients that died in this series were both admitted in a very bad state with dyspnoea, and died within a few days of admission (one within 48 hours and the other within 72 hours). In neither case was there any toxic symptom of the drug or crystals of

TABLE VIII
Results of treatment

Total	Definitely cured	Probably cured (left hospital with no œdema, a trace of albumin in urine but no casts)	Relieved of œdema but left hospital with a little albumin in urine and stray casts	Passed into sub-acute stage	Died
<i>Sulphanilamide treated series</i>					
21	12	3	3	1	2
<i>Control series</i>					
19	7	1	7	2	2

TABLE IX
Speed of cure

Cured within	10 days	3 weeks	6 weeks
Total 15 cures in first series (72 per cent).	10	4	1
Total 8 cures in control series (42 per cent).	2	5	1

acute exacerbation, the end results of the other 21 cases are summarized in table VIII.

sulphanilamide in the urine, though there was marked oliguria in both. Crystals were looked for in the urines of all the cases but not found; other toxic manifestations of the drug were not encountered. One of the cases (no. 18) had a hard cirrhotic liver with jaundice in addition to the acute nephritis, and it is noteworthy that no toxic symptoms developed as a result of the drug.

Case 1 of the series, worthy of mention in detail, was a girl of 11, admitted with generalized œdema of 4 days' duration, smoky urine, albuminuria

with renal and blood casts. The only discoverable aetiological factor was a septic tonsillitis. She did not improve under ordinary therapy; but after a month and a half in hospital she was in a condition of nephrotic nephritis (with massive oedema and albuminuria, low serum albumin and an albumin globulin ratio of 1 : 0.85 in the blood). At this stage she was put on sulphanilamide for 6 days, and the tonsils were thereafter removed under general anaesthesia. She made a slow recovery and left hospital free from oedema, but with a leaky kidney. There was no flare up after tonsillectomy which many modern authorities anticipate. This was probably because of the preliminary chemotherapy.

Comment

The end results in this small series of acute glomerular nephritis in which sulphanilamide has been exhibited compare favourably with the control series as well as the figures given by the American and British writers for nephritis treated without sulphanilamide. Cass (1939) studying 88 cases in England found that the condition ultimately became a chronic one in 32 per cent of those who have not died in the acute attack. Snoke's figure (Snoke, 1939) for a large series of cases in San Francisco was 47.2 per cent while Murphy and Peters (1942) reported the following outcome in 205 cases studied during a ten-year period, 12.6 per cent died during the acute stage; 17 per cent were discharged recovered but were not re-examined; 34.1 per cent recovered and were found healed on re-examination, 9.2 per cent were found latent upon re-examination and 28.8 per cent became chronic nephritics. In the present series, it is noteworthy that 72 per cent left hospital apparently normal in all respects though only a few of them could be followed up. Similar good results have been reported by Williams, Longcope and Janeway (1942) who used sulphanilamide in 42 patients in the acute stage of nephritis, nearly all of them being patients from whom hæmolytic streptococci had been isolated. It may also be mentioned that while the consensus of medical opinion seems to be to wait for a 4 to 6 months' period before removing foci of infection for fear of a flare up (Goldring, 1941) in the one case in which tonsillectomy was done in the present series after preliminary chemotherapy the result was decidedly beneficial.

Summary

A series of 22 cases of acute glomerular nephritis associated with foci of infection in the skin or throat have been treated with sulphanilamide with favourable results as compared with cases treated on standard lines.

Acknowledgments

Thanks are due to Professor P. Kutumbiah, Andhra Medical College, Professor S. Thambiah, Madras Medical College, Lieut.-Colonel G. R. McRobert, I.M.S., Superintendent, Government General Hospital, Madras, and Major F. A. B. Sheppard, I.M.S., Superintendent, King George Hospital, Vizagapatam, for their kind help and permission to publish these records.

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WEIGHT, HEIGHT AND CHEST MEASUREMENTS IN CLASSIFICATION OF TYPES OF INDIVIDUALS

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MEDICAL examination for physical fitness for the public service, the army, the navy, the air force and the industry has become a specialistic study. Standards have been laid down for recruitment from time to time based on the experience gained.

The army, the navy and the air force necessarily have very high standards of physical fitness. In routine examination for physical fitness, the height, weight and chest measurements are usually taken. The standards laid down by insurance companies and textbooks cannot be applied indiscriminately to all races alike. They vary with the races and with the geographical boundaries. The average build of the South Indian is different from that of the North Indian.

On examination, a large number of cases did not satisfy the ratio laid down for assessing weight in relation to the chest measurement and height. Various formulæ have been propounded for assessing the weight of the individual, but none of these work true. Of these, the formula—height + chest girth (in deep inspiration) divided by 17 is the least unsatisfactory; but the actual weight was either far short or far above the assessment even by this formula after making a 10 per cent allowance either below or above the scale. Thus although these candidates were otherwise physically fit

they did not satisfy the condition with regard to weight laid down by the formula.

Carefully recorded evidence of 1,762 cases afforded an opportunity to study this matter. Individuals were classified into normal, sthenic, asthenic and mixed types. The following description shows briefly the characteristic of each type.

Category A—normal type

The torso is of moderate length and of moderate breadth. The thorax is full and moderately rounded, the upper abdomen is firm and rounded and in circumference about the same as that taken just above the nipple. The costal border forms an angle from 70° to 80° . The lower abdomen is flat. The spine shows a mild curve forward in the lumbar region. The respiratory phase in these cases is good and the chest expansion is usually 2 inches or more in deep inspiration.

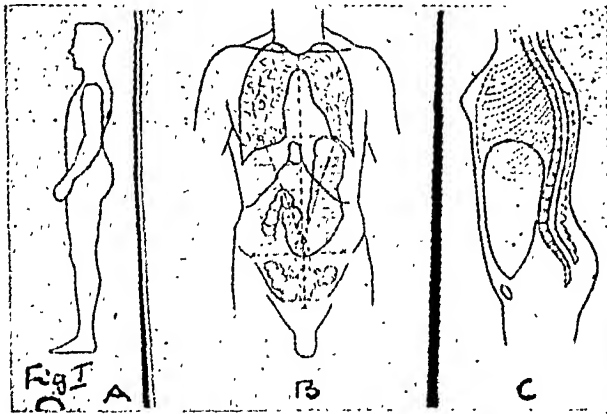


Fig. 1.—Normal type.

A. Side view of the normal human type; note a small forward lumbar view.

B. Corresponds to the description given in the text and shows the position of the organs.

C. Shows the shape of the abdominal cavity, indicating the ample room for fixation of abdominal organs; note the cupola of the diaphragm. The position of organs is ideal and this is the ideal type of man for service requiring executive work.

Category B—sthenic type

In this type there is a preponderant development of the trunk as compared with the limbs. The skeleton is larger and heavier in proportion than in the normal type and the muscles are large with coarse fibres. There is an excess of fat throughout the body but it is bound up with so much connective tissue that it feels hard and firm. The chest is broad, short and deep; chest expansion is large with a wide epigastric angle, 80° to 90° . The abdomen is relatively straight with the pelvis. In these cases the respiratory excursions are more than normal showing an unusual expansion of the chest more than 2 inches during deep inspiration.

Category C—asthenic type

The build is slight; the skeleton is light; the head is large; adenoid and tonsillar tissue are

excessive; the torso is long and is also narrow. The increased length is chiefly in the thorax, the abdomen being relatively short. The sub-costal angle is narrow, there is marked exagger-

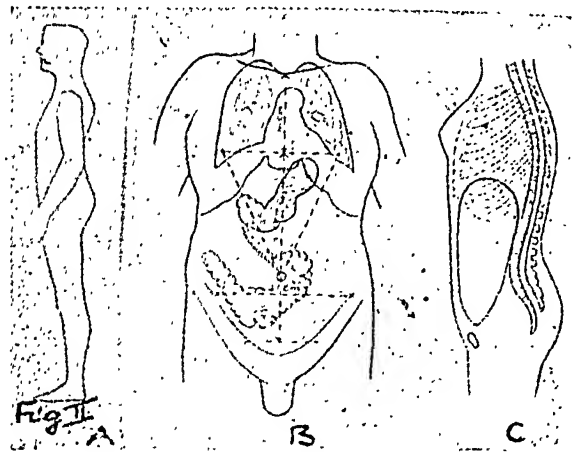


Fig. 2.—Sthenic type.

A. Side view of the broad backed type.

B. Shows the position of the organs and the relationship between the chest and abdomen. Note the wide epigastric angle.

C. Shows the ample capacity in the abdomen for proper fixation of organs. This type of individual is generally suited for heavy work.

ation of the lumbar curve and the feet are slender and highly arched. The respiratory phase is below normal and chest expansion is below 2 inches and is often $1\frac{1}{2}$ inches or less.

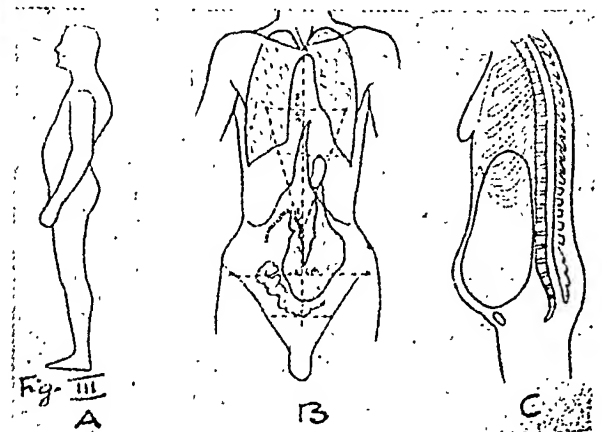


Fig. 3.—Asthenic type.

A. Side view of the narrow backed type—note the relaxed nature of the posture; chin forward, chest back, abdomen forward, marked exaggeration of the lumbar curve, etc.

B. Shows the position of the organs inside—note the low fixation of the organs.

C. Shows that the abdominal cavity is wider below than above. These subjects are liable to constant illness especially if they are selected for executive and heavy labour.

Variations in type occur due to mixtures between A and B, A and C, and B and C. When examining these people it would be necessary to see the preponderating factor present

TABLE
Chart showing height, weight and chest measurement ratio of South Indians

Chest measurement on deep inspiration. Denominator*	28"				29"				30"				31"				32"				33"				34"				35"			
	16	17	19	20	16	17	19	20	16	17	19	20	16	17	19	20	16	17	19	20	16	17	19	20	16	17	19	20	16	17	19	20
Height	102	96	85	81	105	99	89	84	109	102	92	87	112	106	95	90	116	109	98	93	120	113	101	96	123	116	104	99	127	119	107	102
4' 10"	103	97	87	83	107	101	90	86	111	104	93	88	114	108	96	91	118	111	99	94	122	115	102	97	125	118	106	100	129	121	109	103
4' 11"	105	99	88	84	109	102	92	87	113	106	95	90	116	109	98	93	120	113	101	96	124	116	104	99	128	120	107	102	131	124	111	105
5' 0"	107	100	90	85	111	104	93	88	114	108	96	92	118	111	100	95	122	115	103	98	126	118	106	101	130	122	109	104	133	126	112	107
5' 1"	109	102	91	87	112	106	95	90	116	109	98	93	120	113	101	96	124	117	104	99	128	120	108	102	132	124	111	105	136	128	114	109
5' 2"	110	104	93	88	114	107	96	91	118	111	99	95	122	115	103	98	126	119	106	101	130	122	109	104	134	126	113	107	138	130	116	110
5' 3"	112	105	94	90	116	109	98	93	120	113	101	96	124	117	104	99	128	120	108	102	132	124	111	106	136	128	115	109	140	132	118	112
5' 4"	114	107	96	91	118	111	99	94	122	115	103	98	126	119	106	101	130	122	109	104	134	126	113	107	138	130	116	111	142	134	120	114
5' 5"	116	109	97	92	120	113	101	96	124	116	104	99	128	120	108	102	132	124	111	106	136	128	115	109	140	132	118	112	144	136	122	116
5' 6"	117	110	99	94	121	114	102	97	126	118	106	101	130	122	109	104	134	126	113	107	138	130	116	111	142	134	120	114	147	138	123	117
5' 7"	119	112	100	95	123	116	104	99	128	120	107	102	132	124	111	105	136	128	115	109	140	132	118	112	145	136	122	116	149	140	127	121
5' 8"	121	114	102	97	125	118	105	100	129	122	109	104	134	126	112	107	138	130	116	110	142	134	120	114	147	138	124	117	151	142	125	121
5' 9"	123	115	103	98	127	119	107	102	131	124	111	105	136	128	114	109	140	132	118	112	144	136	122	116	149	140	125	119	153	144	129	123
5' 10"	124	117	105	99	129	121	108	103	133	125	112	107	138	129	116	110	142	134	120	114	146	138	123	117	151	142	127	121	155	146	131	124
5' 11"	126	119	106	101	131	123	110	104	135	127	114	108	140	131	117	112	144	136	121	115	149	140	125	119	153	144	129	122	158	148	133	126
6' 0"																																

TABLE—concl'd.

Chest measurement on deep inspiration. Denominator*	36"				37"				38"				39"				40"				41"				42"			
	16	17	19	20	16	17	19	20	16	17	19	20	16	17	19	20	16	17	19	20	16	17	19	20	16	17	19	20
Height	131	123	110	104	134	126	113	107	138	130	116	110	141	133	119	113	145	136	122	116	149	140	125	119	152	143	128	122
4' 10"	133	125	112	106	136	128	115	109	140	132	118	112	144	135	121	115	148	139	124	118	151	142	127	121	155	146	130	124
4' 11"	135	127	114	108	139	131	117	111	143	134	120	114	146	138	123	117	150	141	126	120	154	145	129	123	158	148	133	126
5' 0"	137	129	116	110	141	133	118	113	145	136	122	116	149	140	125	119	153	144	128	122	156	147	132	125	160	151	135	128
5' 1"	140	131	117	112	143	135	121	115	147	139	124	118	151	142	127	121	155	146	131	124	159	150	134	127	163	153	137	130
5' 2"	142	133	119	113	146	137	123	117	150	141	126	120	154	145	129	123	158	148	133	126	162	153	136	129	166	155	139	132
5' 3"	144	136	121	115	148	139	125	118	152	143	128	122	156	147	131	125	160	151	135	128	164	154	138	131	168	158	141	134
5' 4"	146	138	123	117	150	141	127	120	154	145	130	124	159	149	133	127	162	153	137	130	167	157	140	133	171	161	144	137
5' 5"	149	140	125	119	153	144	129	122	157	148	131	125	161	151	135	129	165	155	139	132	169	159	142	135	173	163	146	139
5' 6"	151	142	127	121	155	146	130	124	159	150	134	127	163	154	138	131	168	158	141	134	172	162	145	137	176	166	148	141
5' 7"	153	144	129	122	157	148	132	126	162	152	136	129	166	156	140	133	170	160	143	136	174	164	147	139	179	168	150	143
5' 8"	155	146	131	124	160	150	134	128	164	154	138	131	168	158	142	135	173	162	145	138	177	166	149	141	181	170	153	145
5' 9"	158	148	133	126	162	152	136	130	166	156	140	133	171	161	144	137	175	165	147	140	179	169	151	144	184	173	155	147
5' 10"	160	150	135	128	164	155	138	131	169	159	142	135	173	163	146	138	178	167	149	142	182	171	153	146	186	175	157	149
5' 11"	162	152	136	130	167	157	140	133	171	161	144	137	176	165	148	140	180	169	152	144	185	174	155	148	190	178	159	151
6' 0"																												

1. Height in inches X chest girth (expanded) in inches $\frac{16}{16}$ = sthenic.2. Height in inches X chest girth (expanded) in inches $\frac{17}{17}$ = normal.3. Height in inches X chest girth (expanded) in inches $\frac{19}{19}$ = mixed asthenic normal.4. Height in inches X chest girth (expanded) in inches $\frac{20}{20}$ = asthenic.

* Varies according to type (see text). Weight in lb. =

in their body mechanics. In mixtures of A and B, the preponderating factor may be that of B or A, similarly in A and C; the preponderating factor may be C with minor qualities of A. So also in B and C or A and B. A study of all these variations is necessary in selecting candidates for different types of work.

Category A or a normal human type.—This type satisfies the conditions of sound body mechanics and is perfectly fit for all public services including police, engineering, forest and excise. This is the ideal type and satisfied the formula laid down; but is not commonly found and forms a small percentage of human beings; it formed only 15 per cent of the recorded cases.

Category B or heavily built broad backed type.—This type of individual is fit for appointments which demand strength, as in the police, forest, engineering and excise services and heavy industry and are to be seconded to category A. These candidates formed 10 per cent of the recorded cases. They did not satisfy the formula even after making the allowance of 10 per cent, but satisfied the formula stated below :—

$$\text{Weight in lb.} = \frac{\text{Height} \times \text{chest girth (in deep inspiration)}}{16}$$

Category C or narrow backed type.—This type of individual may be selected for posts where intellectual aspects of the individual are more important than the physical aspects. They can be selected without detriment for public services of a superior type and also for clerical posts. These individuals were below the weight prescribed and after a study of the relationship of the height, circumference of the chest and weight they have been found to correspond to the formula stated below :—

$$\text{Weight in lb.} = \frac{\text{Height} \times \text{chest girth (in deep inspiration)}}{19 \text{ or } 20}$$

In this type, the chest expansion is usually small. Due to the postural defect, the respiration is more abdominal than thoracic and this accounts for the defective expansion. Before deciding that such a type of individual is unfit for service, it is necessary to give him sufficient time and definite instruction to learn thoracic breathing. This procedure was adopted in several cases with success; and in some within the course of a month and in others in a period of three months, they were able to get the necessary chest expansion to befit them for public service.

Conclusion.—In examining individuals for public service, difficulties are experienced in satisfying the rules concerning the weight as laid down by Government from time to time. Careful records of the cases examined have been kept, and the findings are recorded as a guide to those who have to assess individuals for public services, insurance companies, industrial concerns, etc. A tabular statement is

attached to act as a ready reference: it is possible to assess the type of individual by merely noting the height, weight and chest girth, by referring to this table.

I wish to acknowledge the help given to me by Mr. C. S. Thomas, Clerk, Office of the Surgeon, I District, Madras, in maintaining records.

TREATMENT OF CEREBRO-SPINAL FEVER WITH SULPHAPYRIDINE*

OBSERVATIONS ON 464 CASES

By P. V. KARAMCHANDANI

LIEUTENANT-COLONEL, I.M.S.

Specialist in Medicine, Lahore District

and

GHULAM HAIDER, M.B., C.M.P.

WHEN the senior writer came to this station in February 1943, he was struck with the high incidence of cerebro-spinal fever among the troops stationed in the locality (see graphs 1, 2 and 3). This high incidence was accompanied by an equally high mortality rate. It will be seen from these graphs that there was no correlation between the population of the units and the number of cases; also that the season was not a constant factor. Whereas December and January were the worst months in 1942, April, May and June were the worst in 1943. Since June 1943 when the new method of treatment was adopted, although the climatic factor has remained constant, the incidence of the disease has been almost negligible.

One of the causes of the high mortality was found to be the advanced stage in which the patients came to hospital; indeed quite a good many of them were received in either a moribund or an unconscious state. The first thing that was done, in consultation with the consulting physician, in addition to arranging good ventilation of the living quarters, was to stress on the various units the need for sending immediately to the medical inspection rooms any case of fever that showed such symptoms as intense headache and vomiting. The medical inspection rooms were instructed to give priority to cases which showed a positive Kernig or neck rigidity, slow pulse, mental apathy or tendency to unconsciousness and send them at once to the hospital with the diagnosis of (?) cerebro-spinal fever. The most important measure, however, that was adopted was modification of the method of treatment. Hitherto the routine was to start with 4 grammes of M&B 693 orally and then to give 0.5 gramme three times a day. In the case of unconscious patients the drug was introduced through a Ryle's tube and later continued orally if they recovered consciousness.

* Paper condensed by Editor.

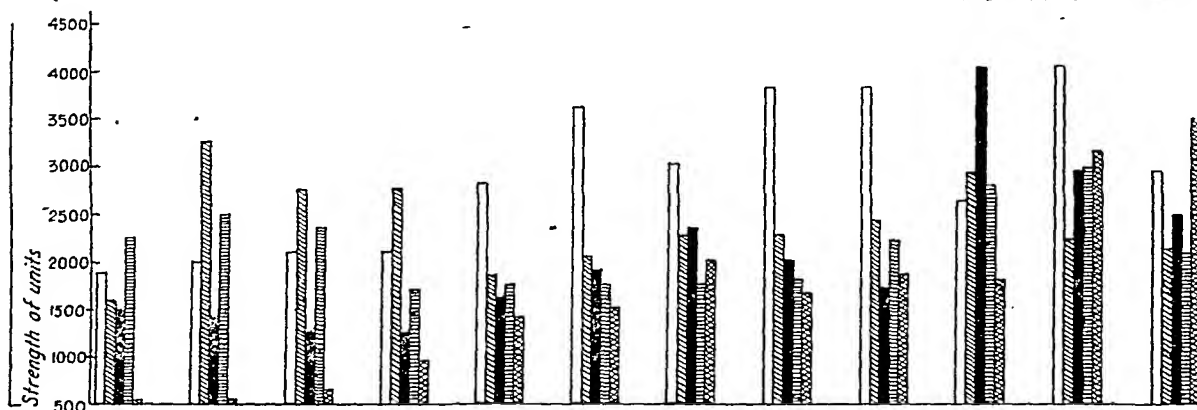
Graph No 1

Strength of units and occurrence of C.S.F. cases during 1942

January February March April May June July August September October November December

References

1. S.T.B.
 2. S.T.B.
 3. S.T.B.
 A SUPPLY.
 B SUPPLY.



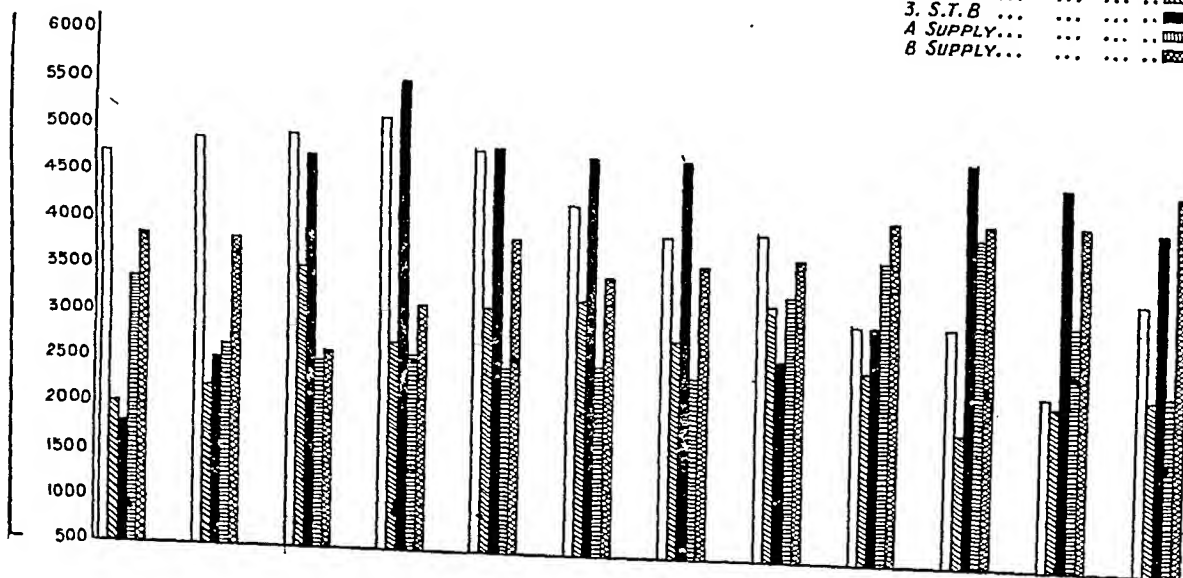
Graph No 2

Strength of units and occurrence of C.S.F. cases during 1943

January February March April May June July August September October November December

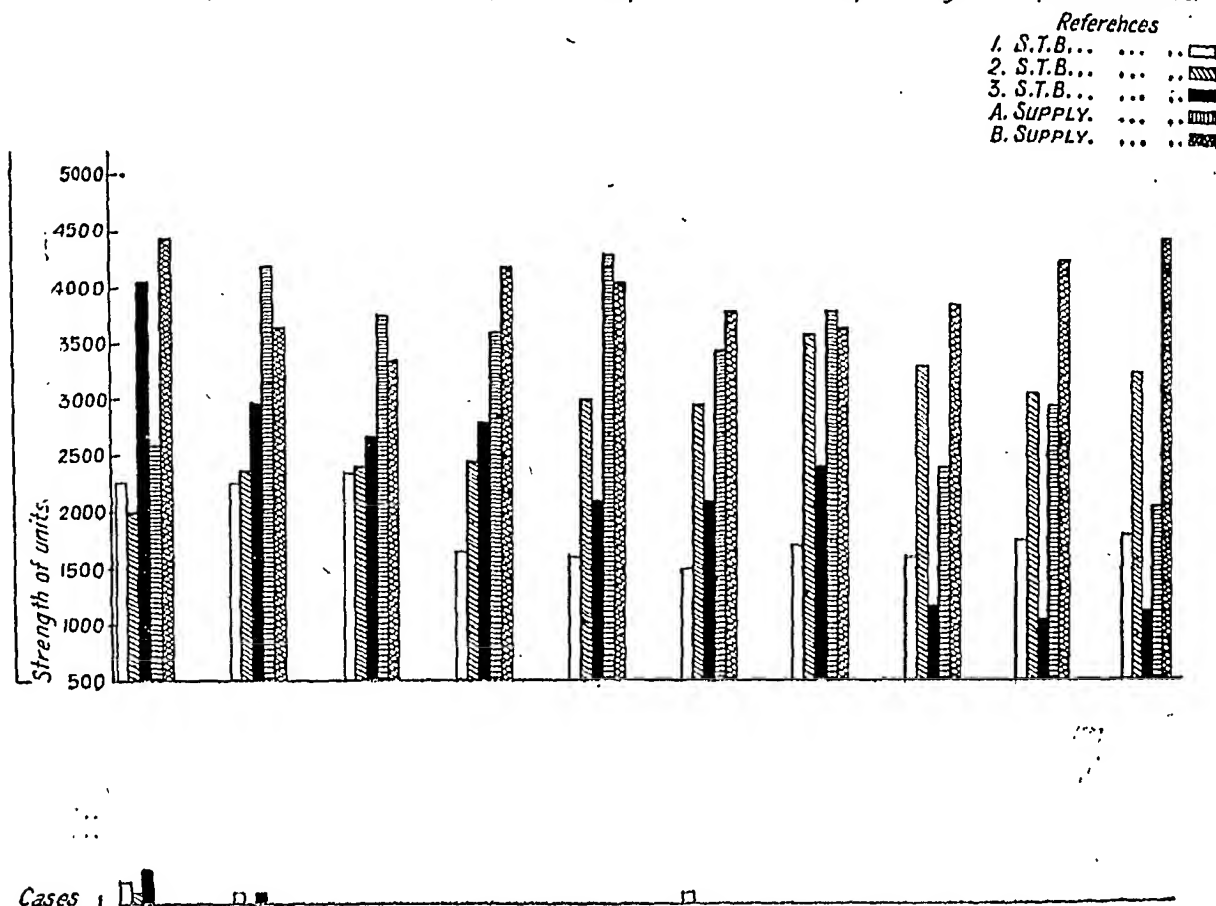
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1. S.T.B.
 2. S.T.B.
 3. S.T.B.
 A SUPPLY.
 B SUPPLY.



Now, the medical officers were instructed to do lumbar puncture immediately after admission | only, whereas it would take nearly 8 hours by the oral route.* That this line of treatment

Graph No 3
Strength of units and occurrence of C.S.F. cases during, 1944
January February March April May June July August September October



and give intravenous injection of one ampoule of daganan soluble one gramme straightway, both to conscious and unconscious patients. Thereafter the unconscious patients were to receive similar injections at intervals of four hours till they regained consciousness, when oral therapy was resorted to. Those who were conscious were given M&B 693 orally after the injection, beginning with 4 grammes and then one gramme four-hourly. This was continued on the average for three days, after which it was reduced by one gramme daily, depending upon the condition of the patient. In addition eight pints of glucose solution were daily given to each patient by mouth.

Although 85 grammes of M&B 693 was the maximum dose administered, the optimum was 31 to 40 grammes. Relapses are likely to occur from premature reduction of the drug, even in cases where the temperature has been normal for three days. Its optimum concentration in the blood should be 10 mg. per cent (Thomas, 1943) and this can almost immediately be obtained in dangerously ill patients by injection

was very successful is shown by the following mortality figures :

1941	14.0 per cent.
1942	18.3 "
1943	January to June	20.8 "
	July to December	9.5 "
1944	6.6 "

* Tentative experiments were carried out in Poona by the senior author with oral administration of sulphadiazine and consequent concentration obtained in blood.

Case A. A single dose of 3 gm. orally. Concentration of 5 mg. per cent was obtained after 2 hours and gradually rose to 8 mg. per cent at the 4th hour and 9½ mg. per cent at the 7th hour after which decline occurred.

Case B. To start with 3 gm. and 2 gm. after 4 hours. Maximum concentration of 11½ gm. per cent was obtained at 8th hour.

Case C. To start with 3 gm. and 2 gm. after 6 hours. At the 6th hour concentration was 9½ mg. per cent, which reached 10 mg. per cent at 7th hour, fell to 9 mg. per cent at 8th and rose to 10 mg. per cent at 9th hour.

Case D. To start with 3 gm. and 1 gm. after 4 hours. Concentration at 4th hour was 5 mg. per cent and reached 6½ gm. at 6th and 7½ gm. at 7th hour.

The effect was equally striking in the case of unconscious patients; thus before June 1943, 20 out of 42 such patients died (47.6 per cent), but later only 4 out of 19 cases died (21 per cent). In some cases, soluseptasine was used instead of daganan soluble, in conjunction with the usual oral therapy, but the results were not so good.

A few miscellaneous points may be of interest. Although the curve of monthly incidence was inconstant and independent of overcrowding, still measures to improve air space appeared to have helped. The diagnosis was based on turbidity of the cerebro-spinal fluid and positive bacteriological evidence. The disease was commonest in recruits of 18 to 20 years of age, but these were also the men who had the lowest mortality. Fourteen cases had malaria as well; quinine treatment had no untoward effect; two of them died owing to severity of the disease and not to malaria. There were four cases complicated with pneumonia, and they all died. Twelve patients who were admitted with symptoms like those of cerebro-spinal fever proved to be cases of malaria.

Conclusions

1. Chances of recovery are greater if the cases be brought under treatment before they become comatose.

2. Every case must receive one injection of daganan soluble one gramme at once on admission, no matter whether he is able to swallow sulphapyridine or not. This gives him a better chance of immediate optimum concentration of drug in the blood.

3. Parenteral therapy must continue unabated in comatose patients till they regain consciousness, when only should oral therapy be restored.

4. Oral administration of M&B 693 should be gradually reduced, even when symptoms appear to subside. Abrupt reduction from one gramme four-hourly to one gramme three times a day carries with it potentialities of recurrence of fever and worsening of general condition.

5. The administration of eight pints of 5 per cent glucose solution orally daily during the entire period of M&B 693 therapy is one of the important details which must not be ignored.

Acknowledgments

Many thanks are due to Colonel B. E. Schlesinger, Consulting Physician, Central Command, and to Colonel K. S. Master, A.D.M.S., Lahore District, for valuable suggestions.

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A Mirror of Hospital Practice

A PATIENT WITH MANY DISEASES

By JOHN LOWE, M.D.

(From the School of Tropical Medicine, Calcutta)

THE general principle of medical practice of trying to explain a patient's symptoms by one diagnosis is a sound one, but particularly in the tropics it is often quite impracticable. Two or even more diagnoses have often to be made.

The case here reported is an extreme example of this.

The patient, an adult male, was admitted to the Carmichael Hospital for Tropical Diseases from the Camp for Sick Destitutes, Narkeldanga, Calcutta, because of poor general condition and œdema of the legs, which was regarded as nutritional œdema. Examination on the day after admission revealed the presence of a large liver abscess, of leprosy patches on the hands and feet, and of the presence of multiple vitamin deficiencies; subsequent examination revealed a heavy hookworm infection and also, later, kala-azar.

The liver abscess was obvious; there was an enormous liver with bulging of the intercostal

spaces, a raised and immobile right dome of the diaphragm, etc. The patient actually had little fever and the total and differential white cell counts were within normal limits. As is not uncommon, the liver abscess was present in spite of absence of a history of amoebic dysentery and the failure to demonstrate *E. histolytica* or cysts in the stool. The liver abscess was aspirated on the day following admission, and three pints of 'anchovy sauce' pus were removed. Emetine treatment was instituted but some fever persisted and also the liver abscess tended to fill again. There was no palpable enlargement of the spleen, but the nature of the fever, the presence of some pigmentation and certain other signs and symptoms suggested the possibility of kala-azar. A complement fixation test was done (WKK antigen) and gave a positive result; sternum puncture revealed *L. donovani*.

Treatment for kala-azar was instituted and the fever slowly subsided. Midway through the course of kala-azar treatment when the patient was afebrile, a second aspiration of the liver was made and two pints of purulent fluid were withdrawn.

The multiple vitamin deficiencies were shown by the tongue and lip changes of ariboflavinosis and the general condition of the skin, dryness, a 'mosaic' appearance and the presence of lichen pilaris, suggesting deficiency of vitamins A and B. A heavy hookworm infection was revealed in routine examination.

On the dorsum of the hand and of the foot were dry and scaly patches of skin showing complete loss of tactile sensibility and thickening of the cutaneous nerves supplying the patch, the dorsal branches of the radial and ulnar nerves in the hand, and the superficial branches of the peroneal nerve in the foot. There was a similar patch on one elbow.

A CASE ILLUSTRATING THE ASSOCIATION BETWEEN CHICKEN-POX AND HERPES ZOSTER

By E. LLOYD JONES, M.D. (Manch.)

MAJOR, I.M.S.

and

J. N. BAHADUR, B.Sc., M.B., B.S.

History.—A Hindu Brahmin lady complained of malaise and pain in the left side of the face and neck from about 23rd February, 1945. On 29th February a rash appeared at the site of the pain, in the area supplied by the 2nd, 3rd, 4th and 5th cervical segments. The lesions were typical of herpes zoster.

On 12th March her little son, aged 2 years, showed feverishness and malaise, and on the following day broke out in a typical chicken-pox rash.

The child, so far as could be ascertained, had not been exposed to infection from any outside source.

Comment.—Walshe (1942) says that herpes zoster stands in some, as yet unknown, relationship to chicken-pox, the appearance of herpes zoster in a family being sometimes followed after an interval of 14 days by a case of chicken-pox. Weismann-Netter and Levy (1938) described a case of chicken-pox which presumably became infected from a patient with herpes zoster in a ward of a general hospital. The converse may take place, and cases of herpes zoster may follow those of chicken-pox.

Herpes zoster is probably a virus infection affecting the cells of the ganglia of the posterior nerve roots of the spinal cord, and it has been suggested by Stern (1937) that chicken-pox and herpes zoster are caused by the same infective agent. The identity of the two infections has been confirmed by Brain (1933) employing a complement fixation test, the serous content of the two lesions providing the antigen.

The connection is of some practical importance when young children are in close contact with cases of herpes zoster, although fortunately chicken-pox is, as a rule, a relatively mild disease. In elderly persons, however, herpes zoster may be a very serious and dangerous condition, and such persons should

therefore avoid contact with children suffering from chicken-pox.

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A CASE OF FRACTURE OF THE BASE OF SKULL RESULTING IN BLINDNESS

By B. L. CHOPRA

Divisional Medical Officer, N. W. Railway, Ferozepore

A GANGMAN was admitted into this hospital on 24th November, 1944, for an injury sustained while he was unloading wooden sleepers, his head having struck against a sleeper. On admission, there was bleeding from the right ear, nose and mouth. Pupil of the left eye showed sluggish light reflex. Severe headache was present, and there was a small contused wound on the skull. He was not unconscious. Slight bleeding continued from all the apertures for about a month. Ophthalmoscopic examination revealed hæmorrhage in his left eye. The optic disc was very indistinct, and the patient had no vision in the left eye. He was, thereafter, sent twice for x-ray examination, but no fracture of the base of the skull was revealed. His eyes were examined for the second time on 22nd January, 1945. Though the hæmorrhage in the left eye seemed to have been absorbed to a certain extent the vision remained nil. The interesting feature of this case is that in spite of having all the obvious signs of fracture of the base of the skull, skiagrams did not reveal any such fracture.

My thanks are due to Dr. C. D. Newman for his kind permission to report this case.

CORRIGENDUM

In the March 1945 issue of the *Indian Medical Gazette*, on page 159, column 1, the formula given for J.S.B. stain as—

Medicinal methylene blue	..	500 c.cm.
Potassium dichromate	..	0.5 gm.
1 per cent H ₂ SO ₄	..	0.5 gm.
Water	..	50 minims

should be as follows :

Medicinal methylene blue	..	0.5 gm.
Potassium dichromate	..	0.5 gm.
1 per cent H ₂ SO ₄	..	50 minims
Water	..	500 c.cm.

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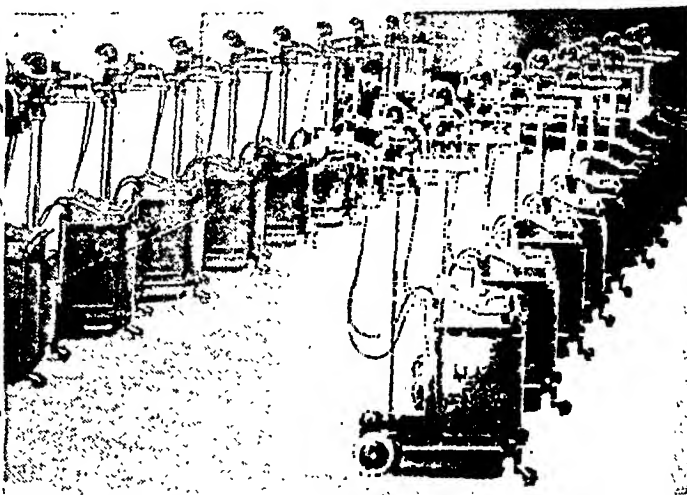
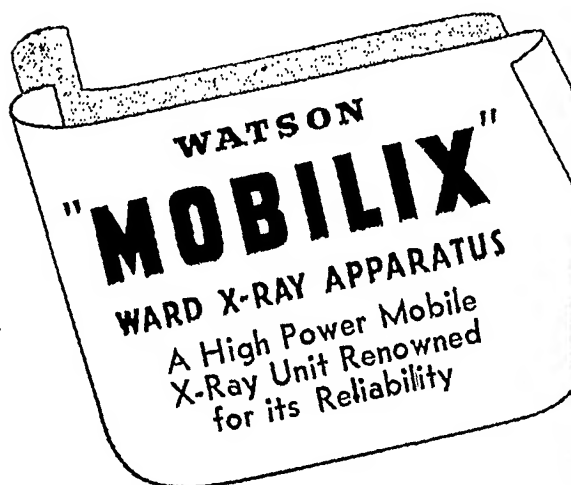
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Indian Medical Gazette

JUNE

RURAL MEDICAL RELIEF

THE recent famine in Bengal has brought into prominence two features of Indian life, viz the low standard of living and the low state of health especially in the village. The situation, bad enough in peacetime, has become worse owing to war conditions, and the future is not encouraging. The state of public health in this country may be summed up in the words of Dr. J. B. Grant, Director of the All-India Institute of Hygiene and Public Health: 'Preventable epidemic diseases, such as smallpox, typhoid, dysenteries, cholera and malaria, are widespread. Tuberculosis is spreading and each year presents a more menacing problem. The resistance of the population to disease is low. Malnutrition and nutritional diseases are omnipresent'. It is therefore not surprising that the general efficiency of the people is low, the mortality rate at all ages is high, and the average expectation of life is not more than 27 years, i.e. less than half that of England. The causes of this state are fairly well known and need not be detailed here. Sir John Orr says that in those born in countries where food and shelter are worst the provision of food and shelter on a healthy standard for every family will double the average length of life. For India this may seem a little utopian even for a hundred years from now, but while freedom from want is a fine ideal, freedom from malaria, dysenteries and other prevailing diseases is equally desirable, and one of our primary needs is to afford free medical services to the indigent people who form the bulk of the population and who live in villages.

Our hospitals were originally built for district and subdivisional headquarters, but these are not easily accessible to the poor people living in villages. Besides, they are few and far between, and can deal with only a fraction of the population. Of late, some dispensaries have sprung up in villages, though often no definite plan is discernible in their distribution. Most of them, however, are primitive, have no beds and cannot be said to be doing much useful work. Some details from one or two provinces might be given as examples of the serious insufficiency that exists in the medical services. In the annual report of the Central Provinces and Berar for 1938, it is said '362 dispensaries are available for a population of over 15 million living in 40,000 villages spread over 98,730 square miles mostly of forest area. This is very inadequate medical relief. The average area covered by a dispensary comes to about 273 square miles while the average

population works out to 42,000 persons'. The 362 dispensaries referred to had only 2,436 beds or one bed for 6,160 persons. Bengal has, it is true, a larger number of dispensaries, but in view of its large dense population (60 millions), their number and accommodation are both inadequate. In 1940, as pointed out by Dr. B. Das in our April issue, outside the Calcutta area, the province had only one dispensary available for an average population of 30,000, and most of these dispensaries had no beds and dealt only with out-patients. The same picture is more or less true of other provinces, with the possible exception of Madras which seems to be following a more progressive policy.

The average budget for medicines and appliances in a rural dispensary, as quoted by Dr. Das, often amounts to no more than Rs. 300 to Rs. 600 a year, whereas the total attendances including new and old cases may be as many as 30,000 or 60,000. This state of affairs lends support to the popular belief that a charitable dispensary gives nothing but 'water'.

Meanwhile a change is coming over the villages, and there is a growing demand for medical amenities. Even the poor people are going to doctors, where available, but this simply adds to their indebtedness which is perennial. Prolonged sickness usually means disaster to their families. Apart from this, the village doctors are handicapped in many ways, especially in dealing with major illnesses; hence it is not unnatural that the people are becoming more hospital-minded, but to get into hospitals is not an easy problem to them. The remedy is to make medical facilities more easily accessible to them, or, in other words, to build up a network of rural hospitals throughout the country.

Those who deplore India's attachment to pre-scientific medicine forget that facilities for scientific medicine are not available to the mass of the people. It is likely that more qualified doctors would settle down in villages if there is a background of hospitals of fairly high standard. In building them up, quality rather than quantity should be the aim, and their distribution should be guided by local requirements and not by local influence. Their present haphazard growth is neither efficient nor effective; it must be superseded. Buildings, beds and equipment—apt always to bulk large in the administrative mind—need not be costly; they are less important than the men who will have to work with them, but the discouraging buildings now in use in many places should cease to exist. Let the hospitals present a neat appearance with compounds, gardens and buildings not too crowded together. They must be provided with adequate beds for both males and females, so that urgent and important cases may be treated as in-patients and of course they should be given sufficient staff and supplies. Laboratory services should be available, and if possible, accessible to the private practitioners,

and a beginning should be made in maternity and child welfare work by attaching midwives whose main work should of course be of a domiciliary nature. Public health services should as far as possible be built up from these hospitals.

If they are to function well, there must be liaison with the district headquarters and sub-divisional hospitals, for patients will come requiring treatment that can only be given in better equipped hospitals and, unless such opportunity exists, there will be stagnation. This of course means provision of additional accommodation in these hospitals, for most of them are even now without sufficient beds. Lastly, it is most important that they should be carefully supervised and regularly inspected.

In our April number, there appeared an article in which Dr. A. T. U. Simeons described a newly-introduced plan for medical relief in Kolhapur State according to which the Government supplies some common medicines—in tablet form or in ready-packed powders—to villages of over 1,000 inhabitants or groups of smaller villages and these are issued to patients by suitably-trained laymen according to instructions contained in a booklet. It is still in experimental stage. We daresay there is room for such 'rural sub-dispensaries' but for obvious reasons they can only be regarded as complementary to the scheme outlined above.

It is well to bear in mind that over ninety per cent of the inhabitants of India live in villages, with agriculture as their main pursuit, and on their prosperity, well-being and working capacity chiefly depends the economic progress of the country as a whole. But ill-health and malnutrition are widespread among them; between 100 and 200 million people suffer from malaria every year, and there is a host of other diseases as well, which take their continued toll of life and health. These people have hitherto been largely neglected. The first of all needs in India, as Professor A. V. Hill recently said, is better health, and to this end the medical and public health services must be greatly strengthened. A glimpse of what Russia has achieved in this field may be gathered from an address given by S. A. Sarkisov, Professor of Neuropathology at the Moscow Institute of the Brain, and Representative in Great Britain of the Red Cross and Red Crescent of the U.S.S.R., a summary of which appears on page 312 of this issue. Our own health problems are immense, and must be tackled on a bold plan. It is time to do away with old methods and traditions.

R. N. C.

SCIENCE AND INDIA

OUR readers may remember the recent visit to this country of Professor A. V. Hill, F.R.S., to advise the Government on scientific research which is now acknowledged to be equally indispensable in peace and war conditions. Pro-

fessor Hill holds an eminent place in the field of science, and his speeches and criticisms are marked by a refreshing candour and originality. We believe he is genuinely interested in the welfare of India, and his interest has not ceased with his return to England, as evidenced by the lecture he gave as Messel Medallist to the Society of the Chemical Industry in which he spoke on the important part that science could play in the development of this country, a summary of which appeared in the *Discovery* of November 1944.

There is, he said, a real interest in science among thoughtful people in India and a widespread conviction that science and the scientific method deliberately and resolutely applied to national development, may be the saving of their country. They realize that scientific development, in the present state of Indian resources, is possible only by co-operation, and they want to co-operate. A close and friendly partnership between the scientists, the doctors and the engineers of Britain and India might result in the application of knowledge to man's urgent practical needs for health and comfort, and, incidentally, succeed in repairing the damage done by treating the problems of India far too long as mainly political ones, instead of being chiefly concerned with the betterment of the life of its people.

Of the progress of Indian science, Professor Hill said it was hopeful; while in India, he frequently heard of bitter complaints about the slowness of progress, the poverty of the universities and institutions, the lowness of salaries, the under-staffing of laboratories, the shortage of proper equipment, and particularly the lack of contact with the outside scientific world. But at the same time, it must be admitted that in the last twenty-five years Indian scientific progress has been greater than in the whole of the previous century.

It is true enough, he said, that only a beginning has been made. The universities and medical colleges are mostly very poor, the latter being mostly staffed by part-time teachers chiefly occupied in practising medicine to earn a living; many laboratories, particularly on the biological side, are under-staffed and ill-equipped; endowments are few and far between, and standards are, on the whole, low. Only a very small proportion of the population are literate in English, which is the language of science in India. There is a common idea that the Indian mind tends rather to dialectic than experiment, to literary, legal or philosophical studies than to practical science or technology. Professor Hill doubts if this tendency is more than an unfortunate accident, due partly to the fact that such studies are cheap and easy, requiring nothing more than lecture-room and books, while practical science and technology are costly in laboratories and equipment. Recent experience in training youths for the technical branches of the Indian forces has shown astonishingly satisfactory results, and

a visit to such places as the Meteorological Observatory at Delhi, or the Tata Steel Works at Jamshedpore, proves that Indian scientists, artificers and operatives can show a high degree of skill, dexterity and workmanship.

India's fundamental needs, he continued, are however in the biological field touching on population, health, nutrition and agriculture. It is more regrettable, therefore, that the biological sciences are so weak and that provision for teaching and research in them is generally so deficient. While not under-estimating the value of physics, chemistry, metallurgy and engineering, he would first strengthen and expand education and research in these sciences, in medicine and its associated subjects, in physiology and biochemistry, in zoology, botany and genetics, and in all the applications of biology to fisheries, agriculture, public health, pest-control and plant diseases, forestry and so on.

He had something equally frank to say to the Indian industrialists who are not unmindful of what science can do for them, but 'on the whole they tend rather to expect other people, particularly the Government, to supply the science while they supply the exploitation of it. There are few examples, as yet, of real research done by industrial firms in their own laboratories, and there are very few examples of endowments for research in universities and elsewhere, provided by Indian industry'.

In conclusion, Professor Hill gave the outline of a plan for research in India. Under a member of the Viceroy's Executive Council, he would set up a system of six research boards, dealing respectively with agriculture, health, industry, surveys of natural resources, engineering and national defence. Each board would have a chairman, not a minister or politician, but an eminent scientist or professional man, and members of the boards would be scientific or practical men in their respective fields. If India is to be happy and prosperous, drastic changes must be made in rationalizing scientific research, and the sooner the better.

R. N. C.

Medical News

RESEARCH IN INDUSTRIAL MEDICINE

UNDER the stress of war, with millions working in the industries, there arose in Britain so many problems that in 1942 the Medical Research Council decided to re-constitute the Industrial Health Research Board and set up a new department of industrial medicine at the London Hospital under Dr. Hunter. Within a short time the growth of the subject has been almost romantic and covers such a wide field that it is difficult to define its limits. Recently a conference was arranged when the research workers gave an account of what had been done and what they were going to do, while the representatives of the employers and trade unions put forward their points of view; this was

followed by general discussions. The proceedings of the conference have been published in a small pamphlet, *Health Research in Industry* (H. M. Stationery Office, London, 6d.) from which we give a few points below.

One of the developments of the war has been the study of men in relation to their tasks, the object being to fit them to the machines and sometimes to adjust the machines to the men. This has meant the reversal of the old view that the more uncomfortable a man is, the more efficiently he is likely to do his work. It is now recognized that he can do a job of work better if he has a feeling of safety and comfort. The psychologists are also endeavouring to fit men and women into their right jobs. We have learned from this war that men of mentally lower grade than the average have their proper place in life and that there is no need for them to be placed in positions for which they are unfitted. Equally important, means must be found to hasten the advancement of able men to suitable positions. Dr. Craik gave an account of the investigations that are being carried out at the M.R.C. unit for applied psychology including the effect of discomfort, fatigue and noise on tasks. A study has been begun on the capacities of blinded officers, with a view to their obtaining suitable employment. Dr. Hunter said how some of the problems caused by industrial poisons have been solved in his department. Thus, it has been found that symptoms like those of major hysteria may be caused by a dangerous fungicide—a methyl derivative of mercury and that dioxan poisoning may simulate Bright's disease. Lately, some cases of polyneuritis were found in men working in a chemical factory where an oil that looks like castor oil—tri-orthocresyl phosphate—was being manufactured for use as a plasticizer. This was the oil which in 1930 had contaminated a popular alcoholic drink in the U.S.A., with the result that nearly 20,000 people were paralysed in their feet and hands. But industrial poisons make up only a very small part of the story of medicine in industry. The rehabilitation of the disabled is a vast but not hopeless problem. Henry Ford said that there were more jobs in a mechanized industry for a man without an arm than for a man with two arms. Systematic investigation is going to be made as to what jobs men with valvular disease of the heart can do in factories. Investigations are constantly being made by the board into such widely divergent subjects as sickness absence, night work, boiler makers' deafness, psychoneurosis in industry, etc. Lord Forrester, as an employer, spoke on, among other things, sanitation and hygiene and on the effect of physical environment on health. Mr. G. A. Issacs pleaded on behalf of trade unions for measures to safeguard the workers' health, thus securing their happiness and efficiency. Research would benefit industry as well as the worker. But research, as Sir Edward Mellanby said, is valueless unless put to practical application. Between the two wars the Industrial Health Research Board had supplied the facts relating to such questions as rest and hours of work, avoidance of accidents, ventilation and humidity, lighting and many others. These results were left unnoticed until the war began. Such research is now regarded as essential for development of efficient and healthy industry.

The report shows how much can be done by well regulated research work. Those interested in industrial medicine would do well to read the pamphlet.

THE CAMPAIGN FOR BETTER FOOD

IN this country sufficient information is already available about food and nutrition and what is required is to make it known to the man in the street and go on repeating until he realizes that the food he eats is both unwholesome and inadequate. The Government of India issue popular pamphlets from time to

time, and one of them is a bulletin *Nutrition*, the fourth number of which is before us. It says in simple language aided by illustrations about the effect of milling rice, popularizing wheat, development of fisheries and balanced diet of which the following example is given for a rice-eating adult—rice 10 oz., millets 5 oz., pulses 3 oz., milk 8 oz., vegetables—non-leafy 6 oz., and green leafy 4 oz., fats and oils 2 oz., and fruits 2 oz. It may safely be said that in the majority of households the last five items are either lacking or not enough. An interesting account is given of a canteen in a Bombay cotton mill which supplies midday meals to about 700 workers consisting of dal, cabbage mixed with black peas, rice and dal curry, butter milk, a piece of cucumber, a piece of lemon and chapati, at the cost of two annas per person, and supplying a considerable proportion of the needed calories. India requires considerable propaganda work about food but to be effective it must reach all strata of the society, and in this the Provincial Governments can do a lot by translating these pamphlets into vernacular languages, by making them available to schools and colleges and by various other means.

THE HEALTH SERVICES OF THE SOVIET UNION

(Abstracted from *The Pharmaceutical Journal*, 17th February, 1945, p. 85)

At a meeting of the Pharmaceutical Society of Great Britain, a survey of the health services of the Soviet Union was given by Dr. S. A. Sarkisov, Professor of Neuropathology at the Moscow Institute of the Brain.

He said that the development of the Soviet health services was easily seen by a comparison with Tsarist days. Then, Russia had no health laws, and the measures for fighting epidemics were primitive and inefficient. There were, for instance, only 250 doctors in the whole State who dealt with sanitation. To-day, Moscow alone had 500 such doctors. Under the former regime, bad social conditions and malnutrition led to epidemics, high incidence of minor ailments, and a high rate of general and child mortality. The level of health education among the people was very low.

The Soviet Government (he continued) entered upon a great battle against these conditions. It was a slow battle, and it was only at the end of the first five-year plan that results were seen. The 25 years of the Soviet regime, however, had been characterized by an unprecedented increase in the network of preventive and curative institutions, the public health had improved, and the death rate was lower. In the cities, where there were 93,000 hospital beds in 1913, this number had increased by 1941 to 491,500. In the rural areas there was formerly an extreme shortage of hospitals and clinics, a fact which added to the problems during the Socialist reconstruction of agriculture. The collectivization and mechanization of labour meant that the medical service had to be developed on a large scale, facilities for specialist treatment provided, and district centres instituted.

In 1938, a law was introduced for 'improving and strengthening the rural medical sector'. To-day, a district centre included a hospital, a well-equipped dispensary, clinics for women and children, crèches treatment centres for tuberculosis and venereal diseases, a health education centre, and a mobile dispensary for the use of the doctors during their tours. The tremendous improvement thus effected in rural areas was shown by a few figures. The number of hospitals had increased, for example, by 66.9 times in the Soviet Republic of Kirghizian, 25.1 times in Kazakhstan, and 19.22 times in Georgia. The number of doctors had increased during the quarter of a century of the Soviet regime by 6½ times—there were 130,000 of them in 1941. In comparison with the 13 medical faculties of 1913, they had now 73 high medical educational

institutions. The number of middle medical personnel rose from 37,476 in 1913 to more than 460,000 in 1941.

An outstanding characteristic of our health services pointed out Professor Sarkisov, was the compulsory and extensive use of preventive vaccination and inoculation. The number of bacteriological institutes has been increasing rapidly, and bacteriological preparations are produced in large quantities. In 1940, for instance, 85 times more preventive vaccines were produced even than in 1928, and 25 times more curative vaccines. The main infections have shown a notable decrease since 1913; typhus has diminished by 80 per cent, diphtheria by 75 per cent, and scarlet fever by 55 per cent. Before the revolution there were permanent epidemics of typhus, but now the disease is rare, occurring only in single cases in different regions. For more than 20 years plague and cholera have been unknown, and there is no smallpox.

Here are, briefly, the results of our war against tuberculosis and venereal diseases, which were widespread in Tsarist Russia. In the years 1913 to 1915 the incidence of tuberculosis and the corresponding death rate were very high, 40 persons dying of it in every 1,000 of the population. The creation of a powerful organization to combat the scourge played a distinguished part in reducing both its incidence and the mortality. The incidence decreased by 2½ times between 1913 and 1941, by which years over 1,050 curative and preventive institutions had been set up, and thousands of doctors and nurses specially trained for this work. Of course, the improvement of living and working conditions has greatly contributed to this result.

In Tsarist Russia there were only 12 special curative institutions for venereal outpatients. In 1940, there was a vast network of these institutions all over the country, especially in districts where the incidence was highest, and thousands of medical expeditions have been sent out to the rural localities to fight this menace. The Government issued decrees making examination and treatment obligatory, with good results, and here again the improvement of conditions and abolition of unemployment helped. As a result of these measures, the incidence of syphilis has fallen to one-tenth of its original figure. An important part in the fight against tuberculosis and venereal diseases has been played by special instructors in sanitary education.

An outstanding place in our State is given to the care of mothers and children. The maternity homes and departments in hospitals can now just cope with the requirements. Before the war there were 725 kindergartens in the Moscow region, with accommodation for 49,000 children, and there are now 954, serving more than 70,000 children. The number of children's consultative centres, crèches and milk kitchens has also increased. Whereas Tsarist Russia had almost the highest infant mortality figures in Europe, those of the Soviet Union are among the lowest.

Nor must the important work of the polyclinics and dispensaries be overlooked. A 'polyclinic' is an outpatient institution, with various special departments equipped for physio-therapy, x-ray work and with laboratories of various kinds served by specialists. The dispensaries are combined curative and prophylactic institutions, and have increased tenfold in 25 years, numbering 13,461 in 1941. They work on a unified plan based on the principle of district service. In addition there are many institutions which undertake the work of popularizing the Government's measures for safeguarding health. These are under the direction of the Central Institute of Sanitary Education in Moscow.

As is known, the whole medical and health service is financed entirely by the State, every citizen being entitled to free medical assistance. The expenditure increases from year to year according to the increase of the national income. Thus it increased between 1929 and 1940—the years of the five-year plans—by 15 times. In the various republics this increase was even greater.

Public Health Section

PREVENTION OF SMALLPOX BY
VACCINATION AND REVACCINATION

A CRITICAL STUDY *

By S. C. SEAL, M.B., D.P.H.

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It is nearly a century and half back that Jenner placed the most sure weapon in the hands of people for the prevention of smallpox. While many countries in the world have taken full advantage of this instrument and have either completely or almost completely eradicated the disease there are a few unfortunate ones in which this fell disease, though gradually losing its intensity, is still making its periodic ravages only to indicate the level of the country's public health activities equally with that of people's public health consciousness.

Barring China for which country reliable records are not available, India is at present the main endemic focus in the whole of Asia, being responsible for more than 90 per cent of cases of smallpox. The following is a record of smallpox deaths in British India from 1868 to 1937 (Russell, 1939).

TABLE I
*Smallpox deaths in India per 100,000
population*

1868-77	1878-87	1888-97	1898-1907	1908-17	1918-27	1928-37
131.85	107.31	59.61	36.15	36.30	34.70	24.15

In sharp contrast with this still high prevalence of smallpox in India is its low incidence in Ceylon, an adjoining land where, in recent years, it has seldom attained 1 per 100,000.

The case fatality rate is also an indication of, and varies according to, the intensity of immunization. For instance, the fatality rate in India is nearly 50 per cent while in the United States it was only 0.4 per cent in 1929 and 1930, although 42,282 cases were reported in 1929 and 46,712 in 1930. The fall of the death rate in the city of New York, U. S. A., from the year 1875 to 1936 is also very instructive (table II).

And it appears from a report of the Committee on Immunization including Vaccination (Picken, 1935) in England and Wales that the incidence was rising on account of incomplete public vaccination. In brief, all statistics show that the incidence and death rate in the

vaccinated group are greatly reduced or negligibly small compared with those in the unvaccinated group, and that in some places the

TABLE II
Death rate from smallpox in New York

Years	Deaths	
1875	1,899	} 9 deaths only in 34 years in a population which has come up to 7½ millions.
1901	410	
1903-1912	1	
1912-1928	8	
1926-1936	0 (10 cases only)	

disease has been completely eradicated by intensive vaccination and revaccination programmes, e.g. Germany, Italy, Hungary, Czechoslovakia, Rumania, Switzerland, Japan, Montreal and also in the Army and Navy and the postal department of Great Britain. These facts are well known to all. My purpose in writing this short note is to discuss certain irregularities observed in connection with the duration of immunity following vaccination and revaccination when properly carried out, and to find out to what extent the results of revaccination can be depended upon as a measure of immunity to smallpox.

Bengal has been passing through a very critical period in her life on account of the very unusual famine conditions prevailing in this province since the year 1943. The disease incidence all round has greatly increased, and among the principal diseases ravaging the country at present, viz. malaria, smallpox, cholera, diarrhoea and dysentery and respiratory diseases—smallpox perhaps ranks second or third in its unusual incidence. It has extended well beyond the seasonal limit, and the most perplexing thing in the outbreak is the report from various sources including our own field experience of cases occurring in spite of the revaccination with its normal three types of reactions having been performed well in advance of the incubation period in the contacts and non-contacts.

Similar observations have recently been reported by MacGregor and Peters (1942) in an outbreak of smallpox in Glasgow in 1942, by D'Arcy, Moore and Whetter (1943) and Smith (1943) in an outbreak of smallpox on a New Zealand Hospital Ship and by Coleman (1944) and Jeans, Jeffrey and Gunders (1944). These records emphasize the uncertainty of the degree and duration of resistance which vaccination and revaccination produce to smallpox and stress the need for further studies.

* Read before the Annual Conference of the All-Bengal Public Health Association held at Calcutta on the 23rd October, 1944.

According to the latest information, at least one-fifth of the population in Bengal (12 millions) has been vaccinated or revaccinated within the last few months, and yet the epidemic could not be brought under complete control. Can this be wholly explained by the lowering of the general resistance due to famine? The other factors, however, are:—

1. Potency of the vaccine at the time of inoculation.
2. Technique of vaccination and revaccination.
3. Quantum of infection.
4. Virulence of the virus.
5. Nature of the virus.
6. Aggregation and dispersal.
7. Effectiveness of revaccination to increase the immunity.

Let us consider these factors briefly:—

1 and 2. *Potency of the vaccine at the time of inoculation and technique of vaccination and revaccination.*—

The usual method of testing the potency of the vaccine is by scarification of the shaven flank of an albino rabbit. Several dilutions are used beginning from 10^{-3} to 10^{-7} . At least 10^{-4} must give a confluent reaction to pass the standard test. The New York City vaccine usually has an end potency of 1.6×10^{-5} (1 : 160,000) and any batch showing an end point more concentrated than 4×10^{-6} (1 : 40,000) is rejected. It is also customary in many institutions to issue a batch of vaccine for the general population after it has proved successful in a preliminary test conducted on human beings. However, even if the lymph is sent out after it has passed the proper test, there is considerable chance of its deterioration under the field conditions in the tropical climate. The potency of the vaccine at the time of inoculation is therefore more important than at the time of testing. The only practical means of knowing the potency at the time of inoculation under the field conditions is the success of the primary inoculations; but there is a fallacy in depending fully upon the primary takes because with a vaccine lymph of low potency, say 10^{-4} , the primary vaccination will take and under proper conditions even one elementary body will produce vaccinia in the susceptibles (Parker, 1938), while a vaccine lymph with a potency 10^{-3} may not be of sufficient strength for revaccination purposes, and secondly, the number of insertions is also important in this respect. These facts were primarily brought forward by the Japanese investigators, Kii (1926) and Kasai (1926), who carried out an investigation on the titration of lymph potency in the semi-immune animals. Their results have been more recently fully confirmed by Horgan and Haseeb (1944) both in animals and in human volunteers. These workers found that lymphs of border-line potency, i.e. those which would pass the standard as recommended by the Smallpox and Vaccination Commission of the League of Nations (1928), completely failed to give reactions. In other semi-immune animals (rabbit and sheep) a given dilution of lymph rubbed on to several equal scarified areas of the animals has produced varying results, some areas being completely negative (immune reactions) and others showing scattered abortive papules or vesicles (vaccinoids). There is a striking similarity between these findings and the failures observed in human revaccination in certain individuals. The following are the results obtained by Horgan and Haseeb (1944) in their experimental investigation on 107 recruits of varying immunity status with two vaccines of different potency, viz, one regular vaccine lymph of end potency 10^{-5} and the other, a specially prepared and concen-

trated suspension of elementary bodies of vaccinia of end potency 10^{-7} (10^{-8} ?).

Method of vaccination.—By two linear insertions by means of surgical needle over the deltoid.

(1) *Primary takes.*—No difference whatever could be observed as expected in the degree of reaction of the primary takes of the two vaccines, each giving 100 per cent insertion success rate.

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(3) *Immune reactions.*—There were 26.1 per cent reactors with E.B.'s as against 31.7 per cent with the calf lymph. Although the difference does not appear very significant for a small number of experimental persons there is no doubt that when a very large body of persons are being vaccinated the total number of individuals who are border-line cases or partially susceptible are likely to be passed as immunes when a vaccine of comparatively poorer potency is used.

Thus in the same experiment the importance of both potency and number of insertions has been demonstrated in case of revaccination. The importance of the number of susceptible host cells exposed to the action of the virus has been emphasized by the recent work of Sprunt (1941) who concludes on the basis of experimental evidence that using adequate quantities of virus the larger the number of host cells per virus particle the greater is the possibility of a lesion. In partially immune subjects the optimal conditions for the multiplication of virus in the skin must be still more exacting regarding the area of the insertions and the actual dose of virus introduced into the incision. While in the case of primary vaccination it may be that a minimum quantity of virus and a single insertion are adequate it is not so in case of partially immune persons, i.e. for revaccination.

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It is difficult to avoid some extraneous contamination in the process of the manufacture of calf-lymph vaccine but there are methods already being successfully utilized which keep down the contaminant to the minimum level so that by further manipulation during the process of trituration with glycerine the final product may be made almost bacteriologically sterile. Sometimes, though rarely, there is contamination with a foreign or heterologous virus. It is primarily to avoid these contaminants that Rivers and Ward (1931, 1933, 1935) evolved the tissue culture technique and Goodpasture and Buddingh (1933, 1934) the chick-embryo method of growing vaccinia virus for preparing the vaccine in a purer form. Unfortunately, the calf-lymph vaccine

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It should also be pointed out that if the lymph tubes are kept in a vertical position for a prolonged period the elementary bodies may get deposited at the bottom. Thus those who receive the inoculation from the top part of such tubes get a smaller number of virus particles than those who receive it from the bottom part.

Furthermore, when glycerol is used, care must be exercised in selecting one that will not inactivate the virus. Merck's (P/W/R Analytical Chemicals) glycerol has been found suitable. The vaccinia virus distributed by the New York City Board of Health is prepared on calves, ripened in glycerol at about -8°C . and then treated with brilliant green. The bacterial count is low in such materials which may sometimes be even free from viable organisms.

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Age at which the primary vaccination is performed

It is well known that the best time for primary vaccination from all points of view is infancy between the age 2 to 6 months. Since a large number of children remain unvaccinated in early life, and in many instances primary vaccination is only performed on adults when an epidemic breaks out, a large proportion of the population remains unprotected, or in other words, the herd immunity remains low favouring the frequent occurrence of epidemics.

It has also been stated that the vaccination of adults is unsatisfactory for two additional reasons, viz: (1) the adults tolerate primary vaccination less satisfactorily than do children and (2) the immunity response in adults is of lesser degree than in children (Holmgren and Lindström, 1937). On this account the intensity of herd resistance will also be less satisfactory when primary vaccination is postponed to a later age.

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3. *Quantum of infection*.—Since smallpox is practically always present in almost all urban communities, if not in most of the rural communities as well, either in epidemic or endemic form, the average person is exposed or has chances of exposure to a large quantum of the virus. Having regard to the relationship between the quantum of infection and degree of resistance, the prevailing conditions in this country are such that persons with a small residual resistance will succumb to the disease on account of the massive dose of infection to which they have opportunities of being exposed.

4. *Virulence of the virus*.—Apart from the question of susceptibility of different individuals, Parker's (1938) studies seem to show that the reaction to the introduction of vaccinia virus in measured quantities varies with different strains introduced intradermally, thus demonstrating quantitative differences in different virus strains as regards producing different grades of reaction. However, the qualitative differences in regard to infectivity were not studied.

It has also been recognized that viruses may vary under natural conditions, and that some variations can be deliberately brought about by experimental procedures, e.g. attenuated rabies virus (non-virulent) or rabies 'virus fixe' for the preparation of rabies vaccine, attenuation of yellow fever virus by passage in chick embryo, and so on. The vaccinia virus itself which is used for vaccination purposes can, by proper handling, be produced from the virulent smallpox virus, the causative agent of a highly contagious disease. Also, a dermatropic vaccine virus can be transformed into neurotropic vaccine virus. Similarly, the virulence may be enhanced under certain circumstances (Duran-Reynals, 1929; Gratia and Linz, 1931; Andersen, 1937; Claudé, 1939; Smith, Horgan and Haseeb, 1941); and possibly this may also occur under natural epidemic conditions analogous to the findings of Greenwood *et al.* (1936) in the case of *P. muriseptica* in experimental studies in epidemiology. It is also known that the reverse change, viz, virulent to less virulent, has taken place in the case of alastrim. Is the present large-scale spread of the disease in Bengal partially due to an increased virulence of the organism, and can the latter be termed as 'epidemic strain' after Greenwood *et al.* (1936)? In view of the other factors prevailing, it is difficult to establish that the strain itself is intrinsically of higher virulence without experimental evidence.

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According to the latest information, at least one-fifth of the population in Bengal (12 millions) has been vaccinated or revaccinated within the last few months, and yet the epidemic could not be brought under complete control. Can this be wholly explained by the lowering of the general resistance due to famine? The other factors, however, are :—

1. Potency of the vaccine at the time of inoculation.
2. Technique of vaccination and revaccination.
3. Quantum of infection.
4. Virulence of the virus.
5. Nature of the virus.
6. Aggregation and dispersal.
7. Effectiveness of revaccination to increase the immunity.

Let us consider these factors briefly :—

1 and 2. *Potency of the vaccine at the time of inoculation and technique of vaccination and revaccination.*—

The usual method of testing the potency of the vaccine is by scarification of the shaven flank of an albino rabbit. Several dilutions are used beginning from 10^{-2} to 10^{-9} . At least 10^{-4} must give a confluent reaction to pass the standard test. The New York City vaccine usually has an end potency of 1.6×10^{-5} (1 : 160,000) and any batch showing an end point more concentrated than 4×10^{-4} (1 : 40,000) is rejected. It is also customary in many institutions to issue a batch of vaccine for the general population after it has proved successful in a preliminary test conducted on human beings. However, even if the lymph is sent out after it has passed the proper test, there is considerable chance of its deterioration under the field conditions in the tropical climate. The potency of the vaccine at the time of inoculation is therefore more important than at the time of testing. The only practical means of knowing the potency at the time of inoculation under the field conditions is the success of the primary inoculations; but there is a fallacy in depending fully upon the primary takes because with a vaccine lymph of low potency, say 10^{-4} , the primary vaccination will take and under proper conditions even one elementary body will produce vaccinia in the susceptibles (Parker, 1938), while a vaccine lymph with a potency 10^{-5} may not be of sufficient strength for revaccination purposes, and secondly, the number of insertions is also important in this respect. These facts were primarily brought forward by the Japanese investigators, Kii (1926) and Kasai (1926), who carried out an investigation on the titration of lymph potency in the semi-immune animals. Their results have been more recently fully confirmed by Horgan and Haseeb (1944) both in animals and in human volunteers. These workers found that lymphs of border-line potency, i.e. those which would pass the standard as recommended by the Smallpox and Vaccination Commission of the League of Nations (1928), completely failed to give reactions. In other semi-immune animals (rabbit and sheep) a given dilution of lymph rubbed on to several equal scarified areas of the animals has produced varying results, some areas being completely negative (immune reactions) and others showing scattered abortive papules or vesicles (vaccinoids). There is a striking similarity between these findings and the failures observed in human revaccination in certain individuals. The following are the results obtained by Horgan and Haseeb (1944) in their experimental investigation on 107 recruits of varying immunity status with two vaccines of different potency, viz. one regular vaccine lymph of end potency 10^{-5} and the other, a specially prepared and concen-

trated suspension of elementary bodies of vaccinia of end potency 10^{-7} (10^{-8} ?).

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of the present epidemic in Bengal is different from the one which had been in existence before, i.e. a variant, or a new type. (c) Does the virus usually contain a single antigen or multiple antigens? If multiple, are all the variolar antigens neutralizable by the specific resistance developed by the usual process of vaccination?

(a) The viruses as affecting human beings may be broadly classified as true smallpox (*variola major*), alastrim (*variola minor*), cow-pox and modified vaccinia. In certain countries, *variola major* rarely occurs except in imported cases and amongst contacts, while alastrim, sometimes called 'modified smallpox', occurs in Great Britain and other Western countries with a very low death rate. Human cow-pox is a very mild and rare disease affecting only the dairy maids and others who handle the udders and teats of infected cows. Modified vaccinia only occurs as a complication of vaccination. Some people suggest that the different clinical forms, e.g. non-hæmorrhagic, confluent, hæmorrhagic or toxic, etc., are due to sub-types of *variola major*. However, it has not been clearly established that these clinical types are due to different strains, or that they are due to variation in host resistance.

(b) and (c) Within the last few years difficulties have been encountered from time to time in explaining certain observations, e.g. cases occurring among the recently vaccinated and revaccinated groups of individuals. The Glasgow epidemic of 1942 reported by MacGregor and Peters (1942) is one example. Lately, some cases were reported by Chatterji, from the Campbell Hospital, Calcutta, and Coleman (1944) reported a case of smallpox in a British Army Unit, which occurred shortly after arrival in India and died of hæmorrhagic smallpox. This person was vaccinated successfully in 1940. Such reports naturally raised the question whether there were variolar viruses against which complete protection was not afforded by the usual vaccination. Goyal in the School of Tropical Medicine, Calcutta, suggested some antigenic differences in the strains. There is, also, a type of smallpox in Australia which affords practically no immunity either to *variola* or *vaccinia* and to which *vaccinia* or *variola* affords only incomplete protection (Ledingham, 1925). Since the existence of multiple antigens (L, S and X) has been shown by Craigie and Wishart (1934), Parker and Rivers (1935, 1937) and others, it is probable that the strains may vary in their antigenic make up, sometimes being lacking in one or the other, and sometimes possessing all the antigens together, as we know happens with many of the known pathogenic bacteria. The differences observed from time to time in virulence or epidemic behaviour may be partly explained on this basis without however ignoring the part played by the hosts themselves in the phenomenon.

Thus some facts have now accumulated within the last few years and particularly during this current epidemic, which call for the reinvestigation of the question of the nature of the virus or viruses responsible for such phenomena in order to reorient our ideas, if necessary, according to the results obtained.

Aggregation and dispersal.—This issue is of general importance in all epidemics. Undoubtedly, this has played an indirect rôle in the spread of the present epidemic. Due to the existing war conditions, there has been a regular and free movement of a large body of persons including many susceptibles throughout the length and breadth of the country, involving cities, towns, and industrial areas as well as villages, thus producing conditions favourable to the spread of all communicable diseases, in-

cluding smallpox. In this connection, it would be interesting to obtain figures of incidence of smallpox cases and cases of other communicable diseases among the recruits, trained armies, troops and troop-attendants.

7. *Effectiveness of revaccination in increasing the immunity against smallpox.*

For the purposes of discussion the issue can be divided under several headings, viz:—

(a) Nature and duration of resistance effected by calf-lymph vaccination.

(b) What constitutes a successful revaccination? How is the resistance influenced by revaccination?

(c) Is the nature of reaction to revaccination a measure of resistance of the same character as the Schick reaction in diphtheria?

Immunity.—(a) Rivers (1939) broadly classifies the immunity in virus diseases including smallpox into three kinds, viz, natural, actively acquired and passively acquired as in bacterial diseases. This is expressed by Topley and Wilson, and by Lal as follows:—

Topley and Wilson's classification

Lal's classification

- | | |
|---------------------------------|-------------------------|
| 1. Innate or genetic immunity.— | With tissue resistance. |
| 2. Acquired immunity. | 1. Genetic. |
| (a) Active | 2. Acquired |
| (α) Naturally acquired; | (a) Natural |
| (β) Artificially induced. | (i) Active; |
| (b) Passive | (ii) Passive. |
| (γ) Naturally acquired; | (b) Artificial |
| (β) Artificially induced. | (i) Active; |
| | (ii) Passive. |

Natural immunity.—'It is the state of resistance to infection not dependent upon a previous spontaneous or experimental contact with infectious agents or their antibodies.' Some workers, however, think that the so-called natural immunity is often due to naturally acquired subclinical infection. But the writer doubts whether subclinical infection can actually occur in smallpox.

Again, in certain virus diseases like poliomyelitis, vesicular stomatitis and equine encephalomyelitis, it has been suggested that physiological maturation or physiological states play a part in natural resistance; but this does not apply to smallpox infection to which people of all ages are susceptible unless protected by proper vaccination. Nevertheless, there is undoubtedly a group of persons, though very few, who are refractory to repeated vaccination. These are the cases which require closer investigation and observation. Perhaps, in most instances, it is only a temporary phase, for there have been records of smallpox infection in children who proved refractory to repeated vaccination. For instance, the son, aged about 5 years, of a certain physician of the Campbell Hospital suffered from smallpox, although he failed thrice to take primary vaccination. There is also the classical example of Sir William Osler who, though repeatedly vaccinated, never had a successful 'take'. Supposedly immune, he worked hard in the smallpox wards in the Montreal General Hospital and contracted the dreaded malady (though a mild attack) in 1875. Thereafter he always cited his own case to illustrate the fallacy of the 'non-take' belief as an evidence of immunity. From various observations it is now known that this type of immunity to infection in general is in some manner not infrequently dependent upon species, age, sex, state of nutrition and genetic background of the host and upon climatic conditions, while little or nothing is known regarding the existence of natural antibodies in virus infection; this latter should be a fruitful field for future investigation.

Actively acquired immunity.—Active immunity is a state of resistance to infection acquired by a normal spontaneous attack of an infectious disease, by experimental or intentional production of the disease or the modified form of it or by vaccine inoculation.

Complete protection against the disease may be obtained by recovery from the attack of the disease, and the immunity thus acquired is said to be life-long although there are exceptions. In a recent epidemic at Calcutta, deaths occurred in persons who were pock marked by a previous attack. The persistence of immunity in persons recovered from virus diseases is so striking that it is but natural to seek an explanation for the phenomenon. Also, if it is a rule to encounter a lasting immunity following virus diseases, one should like to know the reason for the exception.

The presence of humoral antibodies, *e.g.* precipitins, agglutinins, complement-fixing antibodies and other neutralizing antibodies, etc., has failed to explain the cause of enduring immunity, at least in vaccinia (Parker and Rivers, 1936). Others have suggested that in certain instances the protracted immunity following virus diseases is due to a prolonged or persistent sojourn of the viruses in hosts once infected. Then what about those who are called naturally immune, and how can we explain the absence of immunity in some virus diseases like the common cold, influenza, etc.? On the whole, the subject is a controversial one, and the writer thinks that the immunity may not be associated with actual persistence of the virus concerned, which is but a temporary or chance phenomenon in certain cases who have already developed immunity and thus more aptly be classed as aberrant carriers. Moreover, nobody has yet reported such persistence of variola or vaccinia virus in any immune animal. Recently, in their experiments to convert dermal vaccinia into neurovaccinia, Smith, Horgan and Haseeb (1941) observed that the vaccine virus (mouse strain) when inoculated intracerebrally into sheep did not survive long but was capable of conferring solid immunity, whereas in rams it survived for a long period in the testicular tissue without conferring any immunity.

Primary vaccination confers immunity which lasts for a varying period in different individuals—generally 5 to 7 years (according to certain workers—10 years) and declines progressively later on. The following records based on Cameron's experience (quoted by Hutt and Thomson, 1935) will give an idea of the case incidence and mortality among the vaccinated and unvaccinated groups by ages (table III):

Su (1944) also studied the incidence and mortality in a smallpox outbreak at Kweilin (Kwangsi, China) in 1940-41 for different age groups of both vaccinated and unvaccinated individuals. In his series the number of cases among the vaccinated was 156 and that among the unvaccinated was 91 and the average case fatality rates were 12 and 37.3 respectively. From this he concluded that the protection conferred by vaccination against an attack of smallpox was very much weaker than its protection against death from infection when contracted. The number of cases below 9 years among the vaccinated group was 21 of which as many as 14

were below 4 years of age, the corresponding figures in the unvaccinated group being 69 and 58 respectively.

TABLE III

Age	VACCINATED			UNVACCINATED AND DOUBTFUL		
	Admitted	Died	Case fatality, per cent	Admitted	Died	Case fatality, per cent
-10	143	2	1.4	1,441	459	31.9
-20	1,218	23	1.9	761	166	21.8
-30	2,675	144	5.3	374	129	34.5
-40	1,861	247	13.3	180	80	44.4
-50	893	174	18.2	102	57	42.5
-60	311	55	17.7	73	31	42.5
	7,101	645	9.08	2,931	922	31.45

Revaccination has therefore been advocated as a routine procedure for all children of school-going age upon entering a primary school, then again when they enter the secondary school and for the third time when they leave the school (*i.e.* every 5 years on average). This procedure is perhaps the minimum requirement and will undoubtedly minimize the chance of contracting the disease but may not make them completely safe (as discussed elsewhere). As a matter of fact a question may be asked whether strictly speaking antivaccinal immunity is exactly the same as the antivariolar immunity. The similarity of the former to the latter is mostly an inference from the observed records, because it is difficult by the practicable experimental methods apart from test variolization in the vaccinated persons, the older observations of Jenner (1798) and Brown (quoted by Morosov, 1938), to determine the immunity to smallpox in terms of vaccinia virus. Ledingham (1935) has shown that though the viruses of variola and vaccinia possess a common antigen, agglutination experiments reveal some differences between them. Generally speaking, vaccinia affords almost perfect protection against variola and alastrim but the protection afforded by variola or alastrim against vaccinia is not complete. All evidence, therefore suggests that persons possessing complete immunity to vaccinia should also be fully immune to smallpox.

Passively acquired immunity.—The immunity in infants up to the age of 3 to 6 months is supposed to be due to the passive transference of immunity from the immune mothers.

Many workers think of antivariolar or antivaccinal serum as a possible measure for conferring passive immunity against smallpox, and the production of antivaccinal serum has also been made possible (Ledingham *et al.*, 1931; Fairbrother, 1932) but it is still doubtful if it can be used as an effective remedy for treatment.

(b) There are usually four types of reaction after revaccination, *viz.*—

- (1) Primary take type;
- (2) Vaccinoid reaction, or what is known as accelerated reaction;
- (3) Immune reaction; and
- (4) Negative reaction or absence of any response.

The immune reactions have been found in the non-immune group (Ellis and Boynton, 1939). Also, Leake in 1927 stated: 'The fact that the reactions otherwise indistinguishable from reactions of immunity may be given by heated vaccine indicates that at least part of

the visible phenomenon which we call the reaction of immunity is due to this inert material and to that extent may be called a reaction of sensitivity. Even true vaccines not infrequently show an early reaction especially if there have been previous unsuccessful attempts at vaccination'. Thus immune reaction is perhaps a misnomer and therefore it is equivalent to a negative reaction. The latter may however be falsely negative under the following circumstances, viz: (1) low potency of vaccine; (2) faulty technique; (3) local immunity; (4) absence of any tissue response to the infection by the virus. The group of individuals belonging to the last category may be susceptible to the disease although they show a negative response to the vaccinia virus. In regard to the question of local immunity some observations have already been made that if the revaccination is performed in the same spot or near the same spot every year the reaction may be falsely negative due to local immunity although in reality the individual may be susceptible. Horgan and Haseeb (1944a) mention that cases have been reported where successful revaccination has followed deliberate inoculation on a different site. These authors also describe 9 cases, 5 of which suffered from repeated vaccinal infection. The lesion acquired developed in these subjects who were considered highly immune as shown by repeated revaccination results. A suspension of the ground-up crusts from one of these cases when rubbed into the scarified belly of a rabbit gave rise to vesicles of vaccinia on the 5th day thus showing that the infection was due to vaccinia virus.

A successful revaccination may be defined as one in which the 'take' undergoes the same evolution of stages as in the primary 'take'. Some workers also consider the 'vaccinoid' take as equivalent to a successful revaccination and designate both these groups as 'positive reactors'. Probably the first group of positive reactors achieve the same margin of safety against the disease as in the case of primary vaccinations, but the second group, i.e. the vaccinoid reactors as well as the false negative reactors, may not be so protected. Some people are however of opinion that revaccination irrespective of the type of reaction causes an increased immunity. The latter statement is perhaps an assumption not supported by complete experimental evidence or critically observed facts, because there have already been several reports of cases occurring among the re-vaccinated groups of individuals within the supposed period of safety. Moreover, it is a common experience that many persons who get revaccinated every year or fairly frequently and show a negative reaction or the so-called immune reaction on the first or second occasion give positive response (primary take) on the second or third occasion. The results obtained by Ellis and Boynton (1939) in connection with their study of the comparative immunizing potency of these types of vaccine, viz: (1) River's, (2) Goodpasture's and (3) calf-lymph vaccine are interesting. Of the 9,086 medical students selected for experiment, 83 per cent gave a history of being successfully vaccinated before. They were divided into three groups for testing the three vaccines. The distribution of immune reactors among them on the first occasion was as follows: (1) 85 per cent, (2) 64.5 per cent, and (3) 57 per cent. The follow-up of these cases during the next two years yielded the following results: with (1) immune reaction—71 per cent, no reaction—29 per cent; with (2) immune reaction—63 per cent, accelerated reaction—7 per cent, primary take—20 per cent, no reaction—10 per cent; with (3) immune reaction—70 per cent, accelerated reaction—5 per cent, primary take—15 per cent, no reaction—10 per cent. Similarly, Coleman (1944) reports that in response to revaccination 47 (5 per cent) out of 938, the whole contingent in an army unit gave the reaction of primary take in 1943 although the vaccination state of the unit was as follows: 47 men were revaccinated in 1939, 713 in 1940, 56 in 1941 and 122 in 1942. Thus if revaccination giving immune reaction was followed by an increase of immunity, the same cases would not have come down with positive reaction within such a short time.

Smith (1943) made this interesting remark in connection with the outbreak of smallpox in a New Zealand Hospital Ship in April 1943. 'On the ship, as elsewhere, were numerous sceptics who following several unsuccessful vaccinations after an infancy "take" were fully convinced of their immunity until a glorious new "take" developed and shook their faith.'

The author is convinced that immunity to smallpox is relative, and that in certain cases the period of absolute protection can be very short. Thus the question remains: how does revaccination affect the immunity to smallpox, and what are the chances of the immune reactors and the vaccinoid reactors—in particular, the border-line cases, being infected with smallpox? It is no longer feasible to carry out test variolization, but Muller (1932) who studied the problem by observing the results of revaccination carried out on patients during the incubation period of smallpox concludes that it is wiser to assume, to be on the safe side, that although the chances are small, the vaccinoid reactors may contract modified smallpox under certain conditions, e.g. intensity of exposure to variola virus such as is liable to occur during epidemics. It may, however, be said that the negative or immune reaction is almost a certain proof that the individual is immune at that particular time provided that the persons are revaccinated with a very highly potent vaccine lymph and at least two or more than two insertions have been made under strict technical details, and if the reaction is not falsely negative due to the absence of tissue response in the individual. It would also be a wise policy not to select the same skin areas year after year for revaccination.

In terms of this statement let us now examine the results of cases in the recently reported outbreaks in which revaccination had been carried out with successful takes in many cases not long before the attack.

Glasgow epidemic of 1942 (MacGregor and Peters, 1942)

The ship cases were vaccinated on the first to the fifth days of the incubation period, with 6 out of 10 cases giving successful vaccination, and yet contrary to the general expectation they got the disease. Similarly among the 25 city cases, 5 out of 7 cases giving successful vaccination on the 2nd to the 4th days of incubation period suffered from the disease. But perhaps the more important point is the occurrence of cases among those who gave negative or immune reaction, thereby casting doubt on the statement made regarding the value of the immune reaction in indicating complete protection against the disease. Two more cases, nos. 8 and 10 of the ship cases, are also interesting. Case 10 who gave a negative reaction on primary vaccination on 29th May, 1942, was attacked with smallpox within the following week, while case 8 who gave a negative reaction on 29th May, 1942, was successfully vaccinated on 11th June, 1942, only 13 days later, and yet he was attacked within the subsequent 12 days. No doubt, these are exceptional cases but need to be explained.

Outbreak on a New Zealand Hospital Ship—April 1943 (D'Arcy et al., 1943)

Case 1.—Fatal—onset 15th April; was never vaccinated successfully.

Case 2.—Onset 24th April; successfully vaccinated in 1940 and revaccinated on 20th April showing immune reaction.

Case 3.—Onset 30th April; vaccinated in infancy and revaccinated in January 1943 and again on 21st April (unsuccessful).

Case 4.—Onset 1st May; vaccinated in 1940 (scar present), revaccinated on 20th April with immune reaction.

Case 5.—Onset 2nd May; several unsuccessful attempts at vaccination had been made during the past three years but finally successfully vaccinated on 21st April.

The above records show that the first case occurred in one who had been refractory to vaccination. This may be one of the examples of cases in which there is absence of tissue response against the vaccine virus. Cases 2, 3 and 4 gave immune reaction and yet suffered from the disease. Case 5 was within the incubation period and though successfully vaccinated he could not develop complete protection against infection.

Small outbreak reported by Jeans, Jeffrey and Gunders (1944)

Case 1.—Vaccinated in childhood (1 scar), revaccinated successfully at start of epidemic—9 days before symptoms.

Case 2.—Vaccinated in childhood (4 scars), revaccinated unsuccessfully in 1941, and with immediate reaction at start of the epidemic.

Case 3.—Never vaccinated.

Case 4.—Fatal case—successfully vaccinated in the Army in 1943.

These cases are only further examples of what has been reported above.

In view of the above and other observations, it is pertinent to discuss whether revaccination ending in immune reaction actually reinforces the immunity. Since in immunization against bacterial diseases by means of killed vaccines, revaccination always pushes the immunity up, it may be a general belief that smallpox revaccination must behave in the same way. Blaxall (1930) however remarked: 'This operation (revaccination) has the great advantage that if the immunity is low the test inoculation will strengthen it, if high there is no discomfort to the patient.' Very recently, Horgan and Haseeb (1944) also have stated that revaccination in positive reactors (primary and vaccinoid takes) is a method for reinforcing the immunity. But they made no specific remark about the immune reactors. In view of the findings recorded above, the writer is of opinion that there is no increase of immunity in the immune reactors after revaccination; an immune reaction simply indicates that the residual immunity in such persons is above certain critical level, not yet defined, as in the Schick test in diphtheria or Dick test in scarlet fever.

So long as the level of immunity does not fall below this critical level, the revaccination or, for that matter, vaccination, does not take, i.e. it gives a negative reaction (immune reaction is perhaps a misnomer). Thus it is possible that those people who are practically in the border line may soon lose their immunity and become susceptible to the infection. The vaccinoid reactors may accordingly either be the border-line cases or have just passed beyond the border line, and are therefore nearly as much susceptible to smallpox as the group belonging to the primary takes. Indeed, these are important issues for further investigation. It is, however, needless to say that if the reaction is like a primary take, one should be as sure of immunity such as is conferred by primary vaccination, except perhaps in those who are inoculated within the incubation period.

Finally, Horgan and Haseeb (1944) claim that the revaccination carried out properly, as

they have defined, gives a better measure of immunity against smallpox than the serological methods which, as some of the workers have stated, do not seem to run parallel with the actual immunity status of the individuals. But unfortunately the latter has never been clearly defined nor the question of critical level specifically studied. Since there are many factors on which the success of revaccination depends, the results of revaccination are only a rough measure of the immunity status but the serological methods once standardized will certainly be a better guide for the problem. There are therefore sufficient reasons for carrying out extensive and critical studies of the available serological methods along with fresh attempts at exploration of the newer fields of attack particularly in the neutralization technique and animal experimentation methods.

In this connection, the recent editorial comment in the *Lancet* (1944) may be recalled: 'Opinion is hardening that vaccination after exposure, however early, cannot be relied upon. Leishman (*J. R. Army Med. Corps*, 1944, 2-58) reporting the management of smallpox in an India-based general hospital goes so far as to state that vaccination even early in the incubation period may aggravate the disease if it fails to prevent it. Vaccination, like other forms of active artificial immunity, produces in the healthy subject an immunity of variable duration; repeated revaccination is essential if immunity is to be maintained, and even revaccination every five years may be inadequate for some. With vaccination after exposure the question is whether the artificial immunity induced by the vaccination can successfully race the progress of the disease in the incubation period. If done early, it usually can. By analogy with other *infections de rappel*, revaccination is likely to be more rapid and efficient than primary vaccination, but there are now plenty of examples of failure to prevent the disease by vaccination early in the incubation period. If vaccination is not to fall into further disrepute its limitations must be accepted.'

The question may finally arise what should then be the procedure in public health to give as complete a protection against smallpox as possible. The answer probably is that mere completion of the quota of primary vaccination will not give us the security sought for, because the primary vaccinated groups as they grow in age constantly add to the number of susceptibles which when accumulated beyond a certain critical point may institute an epidemic, or in its absence, sporadic cases leading to endemicity. Revaccination with known highly potent lymph should therefore be as much intensified as the primary vaccination, and should be made compulsory as in Germany, Italy, Rumania, Japan and other countries where smallpox has been practically eradicated. Otherwise, incomplete primary vaccination supplemented by incomplete revaccination will

lead the country to the stage in which we are in at present, or with more intensive primary vaccination and partial revaccination the country may come up to a position now held by countries like Great Britain and U. S. A. in which smallpox epidemics still occur though not commonly. The aim of the public health administrators in India, I believe, is at least to achieve the latter position for the present, but it may reasonably be expected that they have the question of compulsory or intensive revaccination in view as a programme of the public health reconstruction scheme which is at present undergoing the process of hatching.

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Current Topics

Treatment of Human Anthrax with Penicillin

By F. D. MURPHY
A. C. LABOCETTA
and
J. S. LOCKWOOD

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXVI, 9th December, 1944, p. 948)

1. THREE cases of uncomplicated cutaneous human anthrax without bacteremia were treated with penicillin. As far as we know, this is the first report on the use of penicillin in the treatment of patients with cutaneous anthrax.

2. Exceedingly prompt and excellent clinical response to penicillin was observed in every case.

3. Bacteriologic studies showed that there was rapid disappearance of B. anthracis from the cutaneous lesions after administration of penicillin.

4. In vitro studies of the strain of B. anthracis isolated in one case showed it to be sensitive to the action of penicillin, but one hundred times less sensitive than a strain of *Staphylococcus aureus*.

5. A total of 100,000 units of penicillin is certainly the minimum effective dose, and a total of 200,000

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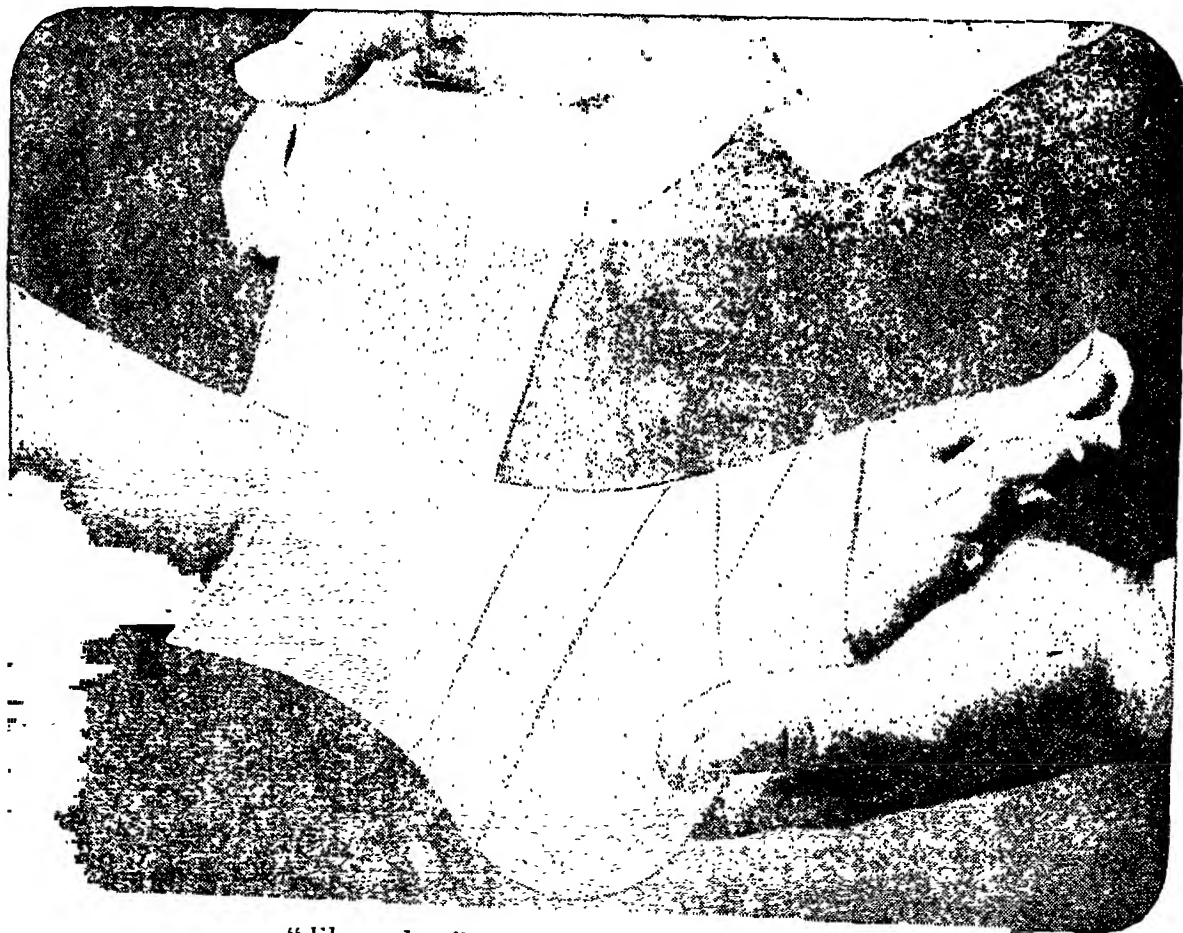
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to 400,000 units, given at a rate of 100,000 units per day, should serve to evoke a satisfactory therapeutic response in the average uncomplicated case of cutaneous anthrax.

6. Penicillin is a valuable agent in the treatment of human anthrax and deserves further clinical trial in this disease.

Proteolysed Liver in the Treatment of Refractory Anæmias

By L. J. DAVIS

and

L. S. P. DAVIDSON

(Abstracted from the *Quarterly Journal of Medicine*, Vol. XIII, April-July 1944, p. 53)

1. AN account has been given of the response to oral proteolysed liver in 13 cases of severe anæmia which had proved refractory to treatment with injections of liver extracts of known potency.

2. In five of the cases the morphology of the peripheral blood and sternal marrow was respectively macrocytic and megaloblastic and was typical of Addisonian pernicious anæmia, although only one of the cases conformed fully in other respects to the usual diagnostic criteria for this disease.

In all these cases the administration of proteolysed liver resulted in a prompt and vigorous hæmatopoietic response and the rapid restoration of the patient to normal health.

3. In three other cases the anæmia was also macrocytic, but the sternal marrow films showed 'dimorphic' erythropoiesis. Proteolysed liver in these cases was followed by only partial blood regeneration with the survival of the patients in moderate health.

4. The remaining five cases of anæmia were of the aplastic type with hypocellular normoblastic sternal marrow, and completely failed to respond to proteolysed liver or to any other form of treatment.

5. The significance of these observations is discussed and it is suggested that proteolysed liver contains, in a readily assimilable form, some hæmatopoietic maturation factor additional to the anti-anæmic factor present in fractionated liver extracts.

Penicillin Therapy in Ocular Infections

By J. G. BELLOWS

(Abstracted from the *American Journal of Ophthalmology*, Vol. XXVII, November 1944, p. 1206)

1. PENICILLIN reaches the ocular tissues within a few minutes after intravenous injection.

2. After a large dose of penicillin is administered intravenously, it appears in the ocular tissues listed in decreasing order of concentration as follows: extra-ocular muscles, sclera, conjunctiva, blood, tears, chorioretinal layer, aqueous and vitreous humours, and cornea. It has never been detected in the crystalline lens. In this respect, the lens is similar to the cerebrospinal fluid, brain, and nerve tissues.

3. Local application of penicillin leads to a very high concentration of the drug in the tissues of the anterior segment of the globe.

4. The following four ointments, in which the penetrability of penicillin was tested, are listed in the order in which they are clinically recommended: simple ointment, oil-in-water emulsion, and lubricating jelly. The 'vanishing' stearate type of a base, in which penicillin seems to have the greatest power of corneal penetration, is not recommended because of its possible damage to the corneal epithelium. However, it may be used on the skin of the lids.

5. Penicillin was found to be effective in the clinical treatment of acute and chronic infections of the lids, conjunctiva and cornea produced by penicillin-sensitive organisms.

6. It was found ineffective in two cases of exudative choroiditis of undetermined origin and in one case of gonorrhoeal iridocyclitis.

7. Susceptible individuals may become hypersensitive to penicillin.

Penicillin in Beeswax

(From the *Lancet*, ii, 9th December, 1944, p. 760)

As penicillin becomes more generally available for infections which are not severe enough for treatment in hospital, the need for more manageable methods of administration becomes more apparent. In the Services gonorrhoea is not proving as amenable to sulphonamide therapy as was hoped, and penicillin is replacing sulphonamide as the drug of choice, as well as being required for sulphonamide-resistant infections. The best results in gonorrhoea have been obtained with a series of 5 to 6 injections of 20,000 units at three-hourly intervals. Obviously it would be advantageous to reduce the number of doses if the bacteriostatic effect of each dose could be continued longer than the customary 2 to 3 hours. We have already commented on the experimental use of *p*-amino-hippuric acid to delay excretion of penicillin, apparently by interfering with its passage through the cells of the renal tubule. Another likely method seemed to be the use of an oily excipient to delay absorption from the site of injection. Peanut and other vegetable oils and protamine zinc have been tried for this purpose, but were not very effective. Romansky and Rittman now report experiments with mixtures of peanut oil with beeswax, which has previously been used for prolonging the action of histamine and heparin. USP bleached beeswax was added to peanut oil in proportions from 0.75 per cent to 6 per cent; 2 to 3 c.cm. of the mixture was pipetted into an ampoule of purified penicillin powder, and the mixture was then shaken up with a few beads to ensure uniform dispersion of the drug. Preparations of this kind kept in the refrigerator, at room temperature, or in the incubator at 37°C., retained their original potency for 30 to 62 days. Initial experiments with rabbits showed that after an injection of 5,000 to 10,000 units of penicillin in 1 c.cm. of the oily fluid, an inhibitory level of penicillin was maintained in the blood for 6 to 12 hours compared with 2 hours for the same dose of penicillin in saline. Injections of 41,000 to 66,000 units of penicillin in 2.0 to 2.4 c.cm. of beeswax oil into three human volunteers gave demonstrable blood levels for 6 to 7 hours and penicillin was present in the urine for 20 to 32 hours after the injections. None of the patients complained of local pain or irritation. Because of these findings, 12 patients with gonorrhoea were given one dose of penicillin (unitage not stated) in beeswax oil and 11 of them were cured; 53 others were later cured by a single injection. Further data on this method of administration are promised and are obviously needed.

Penicillin and Spiral Organisms

(From the *British Medical Journal*, ii, 2nd December, 1944, p. 729)

ALTHOUGH penicillin and the sulphonamides cover much common ground, each has fields of activity in which the other takes no part. Perhaps the most important direction in which penicillin is of value while the sulphonamides have none is in the treatment of 'spirochaetal' infections, using that word in its broader and less legitimate sense. The place of penicillin in the treatment of syphilis is now almost assured; if long-term results are satisfactory it may replace the arsenicals altogether, at least for the primary form of the disease. It would be rash to assume that all spiral organisms will react in the same way, since they include a number of widely distinct genera, but scattered items of information are

coming to hand which suggest that some degree of susceptibility to penicillin is a common property among many of them. The rapid disappearance of *T. vincenti* from the lesions of Vincent's gingivitis reported by MacGregor and Long in this journal last week is one such piece of evidence from the clinical field. Others are so far experimental only: an effect on *Sp. minus* and on *T. recurrentis*, first reported by E. M. Laurie and H. O. J. Collier, has been confirmed by F. R. Heilman and W. E. Herrell and by H. Eagle and H. J. Magnuson, respectively. The former authors found penicillin curative in experimental mouse infections due to either *Sp. minus* or *Strepto-bacillus moniliformis*; both forms of rat-bite fever may therefore prove amenable. Eagle and Magnuson, studying infection with *T. novyi* in rats and mice, found that, although 50 per cent of cures could be obtained with a dose of about 100,000 units per kg., 95 per cent cure called for 400,000 units per kg., a dose of which the equivalent in man is about 25,000,000 units. If all species of *Treponema* causing relapsing fever behave in this way, and if findings in mice prove applicable to man, penicillin is unlikely to displace arsenic for the treatment of this disease.

Leptospiral infections must be regarded differently, because arsenic is useless for them. Even should *L. icterohæmorrhagiæ* be only moderately susceptible to penicillin, the treatment of Weil's disease should still be attempted, since there is no chemotherapeutic alternative. Some indications that this treatment may prove useful are to be found in two papers in our present issue. J. M. Alston and J. C. Broom began by determining the concentration of penicillin which would inhibit the growth of 9 strains of the organism in cultures; all were inhibited by 0.4 unit of penicillin in 3.5 ml. of medium—i.e. a concentration of just over 0.1 unit per ml. This is about five times the concentration necessary for preventing the growth of a normally sensitive staphylococcus, but the fivefold dilutions used do not enable an exact comparison to be made between the two organisms. The first therapeutic test failed, evidently owing to infrequent dosage; in the second, penicillin was administered three times a day in oil, with the result that 6 out of 7 treated animals survived, the seventh dying apparently of some other cause, while 4 out of 8 controls died. These findings, although inconclusive owing to the small numbers of animals used, encourage further observations. In the patient with Weil's disease described by V. Lloyd Hart, penicillin was given at too late a stage to judge its effect on the course of the disease, but may have contributed to eliminating the organisms from the urine. So far as they go, these observations justify the clinical trial of penicillin in the treatment of Weil's disease; early diagnosis and perhaps generous dosage will be necessary.

Comparative Amœbacidal Activity of Phenyl Arsine Oxide (Mapharsen), Related Arsenicals and Other Agents

By H. H. ANDERSON
and

T. T. K. CHUAN

(Abstracted from the *American Journal of Tropical Medicine*, Vol. XXIV, November 1944, p. 367)

A study of the amœbacidal activity *in vitro* of mapharsen and seven other compounds and three known amœbacides is reported. Of the group of agents tested *in vitro*, mapharsen was most effective and killed *E. histolytica* in 1 to 20,000 to 1 to 30,000 dilution on 48 hours of exposure. 2, 4-dihydroxyphenylarsenic acid was effective in 1 to 8,000 dilutions against one strain of *E. histolytica* and N, N'-disodiumformaldehyde bisulfite-3, 3'-diamino-4, 4'-di(B-hydroxyethoxy) arsenobenzene in 1 to 3,000 dilution was effective against two other strains. Other drugs had no appreciable effect on amœbæ in similar concentrations.

Water-Soluble Vitamins in Sweat

By F. SARGENT

P. ROBINSON

and

R. E. JOHNSON

(From the *Journal of Biological Chemistry*, Vol. CLIII, April 1944, p. 285. As abstracted in *Bulletin of Hygiene*, Vol. XIX, September 1944, p. 706)

'From a review of the work of those investigators who have employed the most specific methods as well as an acceptable technique in collecting and handling sweat, it is concluded that loss in the sweat is not a significant factor in depleting the body's stores of water-soluble vitamins. Even under severe conditions, loss in the sweat is much less than excretion in the urine.'

The Mode of Action of Sulphonamides

By R. J. HENRY

(From the *Bacteriological Reviews*, Vol. VII, December 1943, p. 175. As abstracted in *Bulletin of Hygiene*, Vol. XIX, September 1944, p. 717)

This review opens with a brief account of the theory of Woods and Fildes that sulphonamide acts by interference with the utilization of *p*-aminobenzoic acid (PABA). 'This theory is based on certain assumptions which have not as yet been proved and, furthermore . . . the observations leading to the main arguments presented for its support can be equally well explained on an entirely different basis, and in fact, in certain circumstances must be interpreted on a different basis. . . . It is considered that sulphonamides achieve their bacteriostatic action by direct inhibition of one or more enzymes, and in the final section of the review the theory is tentatively developed that sulphonamides inhibit cell division by a primary inhibition of one or more of the oxidation-reduction enzymes.'

JOURNAL OF THE MALARIA INSTITUTE OF INDIA

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NOTES ON THE DISTRIBUTION, BREEDING PLACES, ADULT HABITS AND RELATION TO MALARIA OF THE ANOPHELINE MOSQUITOES OF INDIA AND THE FAR EAST

The following is a summary of this article.

The present article deals only with those species recorded in India and the Far East which have either been found naturally infected with malaria parasites

or have been suspected to be vectors of malaria on epidemiological grounds.

The area dealt with includes India, Burma, Thailand, Indo-China, S. China, Formosa, the Andaman and Nicobar Islands, Malaya, the East Indian Archipelago, Northern Australia and certain of the S.-W. Pacific Islands. The East Indian Archipelago includes the Great Sunda Islands (Sumatra, Java, Borneo, Celebes, Banka, Billiton), the Little Sunda Islands (Bali, Lombok, Sunbawa, Flores, Sumba, Timor), the Moluccas, New Guinea and the Philippine Islands. The S.-W. Pacific Islands referred to are New Britain, New Ireland, the Admiralty Islands, the Solomon Islands and the New Hebrides.

As a general rule the mosquitoes of the E. Indies may be differentiated into Asiatic and Australian forms, the line of demarcation passing between Celebes and the Moluccas to the north and between Roma and Damar Islands to the south. This rule is not however absolute, for *bancrofti*, a typically Australian species, has recently been reported on the west coast of Celebes.

More than 100 species or varieties of *Anopheles* have been described from these regions, but the majority have never been suspected to be malaria carriers, and only 41 are included in the present review. Of these, 12 are classed as vectors of major importance and a further 16 of local importance in certain areas. The remaining 13 probably play little or no part in the transmission of malaria in nature.

Among the species listed as vectors of major importance there are two groups which have particularly affected the conduct of military operations during the present war: (i) the *fluvialis-minimus* group which is responsible for the intense malaria prevailing throughout the foothill tracts of India and the northern sector of the Far East from Burma to S. China, and (ii) *punctulatus* and its variety *moluccensis* which play a similar rôle in New Guinea and the S.-W. Pacific Islands wherever the disease is rife.

In the following three articles the author's summary or abstract is given.

PROBLEMS RELATING TO MALARIA CONTROL IN DELTAIC BENGAL

A. philippinensis is the primary transmitter of malaria in the deltaic region of Bengal (excluding the estuarine zone). This is the only species that has consistently been observed naturally infected in this area. High rates of infection have been recorded even under static conditions and its prevalence shows a positive correlation with local malarial endemicity.

The incidence of infection in the mosquito shows a seasonal variation. Infection rates are high from July to December and low from January to June. Sporozoite infections are frequent from July to December and very rare during the remainder of the year. As the prevalence of the vector, the natural infection rates and the frequency of sporozoite infection are high from September to November, this is probably the period of maximum transmission of malaria.

During daytime, *A. philippinensis* rests mainly in houses and only very rarely in cattlesheds. Unlike most other anophelines it rests very close to the floor.

The breeding season of *A. philippinensis* is from July to October. It usually breeds in ponds with clean water free from organic contamination. It prefers sunlit breeding places. Ordinarily it does not breed in small water collections of a temporary type nor in ricefields.

Aquatic vegetation of the submerged type, which reaches the water surface as sub-aquatic bushes, is favourable for the breeding of *A. philippinensis*. The aquatic plant most frequently found associated with it is *Hydrilla*. Plants which grow over the water surface in such a manner as to produce a shade over the water are inhibitory. A dense growth of the water-hyacinth (*Eichhornia speciosa*) controls the breeding of this mosquito effectively. The

inhibitory influence of the growth of *Eichhornia* on the breeding of *A. philippinensis* has been experimentally demonstrated, and appears to be due to the shading out of the type of algal growth that forms the main food of the larva.

The occurrence of certain forms of green algae that constitute the main food of the larva, favours the development of the larva. Certain other algae, such as *Microcystis aeruginosa* and *Euglena*, are unfavourable for the breeding of *A. philippinensis*.

The depth of the water table during the breeding season of *A. philippinensis* has a considerable influence on the prevalence of this species. In the deltaic region, areas with a high water table during the rainy season have a low prevalence of *A. philippinensis*. Areas with comparatively lower water tables show an increasing incidence of this mosquito.

Malaria control measures in the deltaic region should be directed primarily against *A. philippinensis* by the following methods:—

- (i) Insecticidal spraying of dwelling rooms.
- (ii) Control of breeding in ponds and other large water collections by (a) complete removal of all forms of aquatic vegetation, or (b) by stocking the water collections with water-hyacinth so as to form a complete covering over the water surface.
- (iii) Raising the water table through irrigation or by other methods.

THE BEHAVIOUR OF *Anopheles fluvialis*. PART II

From September to November, when the gonotrophic cycle takes 48 hours in the laboratory, wild-caught female *A. fluvialis* from houses in N. Kanara District are in the proportion of 10 of Class B (freshly fed) to 3.5 of Classes C and D (partially-digested blood and partially-developed ova). From December to February when the gonotrophic cycle takes 72 hours in the laboratory, these proportions are 10 of Class B to 5.4 of Class C and 4.1 of Class D. From these observations it is concluded that about 60 per cent of mosquitoes leave indoor for outdoor shelters in the former period and about 40 per cent in the latter period every night.

One male and 16 female *A. fluvialis* (all of the latter having taken a blood meal) were collected during the day from outdoor resting places consisting of clefts in or the undersurface of rocky banks with plenty of undergrowth all round.

Most female *A. fluvialis* in Class C tend to leave the place of their release and, inferentially, their daytime resting places at or soon after dusk and, while none of these specimens was recovered from indoor shelters on the following morning, some of these were recovered on subsequent nights and mornings when or after they had entered tents or houses for purposes of feeding, indicating that these insects must have resorted to outdoor shelters on the night of their release.

Similar experiments with freshly-fed female *A. fluvialis* have shown that most of these leave their places of feeding for outdoor shelters between the time of feeding and dawn.

This behaviour of *A. fluvialis* is discussed with reference to its bearing on the utility and frequency of spray-killing as a method of malaria control and certain tentative suggestions are put forward. In sparsely populated areas in N. Kanara District, daily spray-killing is advocated. In larger areas, combined with antilarval control, a programme of spray-killing twice a week during that part of the malaria season when the gonotrophic cycle takes 72 hours and on 2 consecutive days followed by a break for 2 days during the season when the cycle takes 48 hours is recommended.

Approximately 71 per cent of *A. fluvialis* were found to enter houses for feeding during the first quarter after dark, 19 per cent in the second quarter, 7 per cent in the third quarter and 3 per cent in the last quarter.

LABORATORY STUDY ON THE LARVICIDAL ACTION OF A MINERAL OIL LARVICIDE WITH SOME OBSERVATIONS ON THE PROBABLE EFFECT OF FIELD CONDITIONS

The maximum effect of a 10μ film of a sample of a proprietary larvicide (Larvicide A) was exerted in 10 minutes at 31°C ., when the percentage of larvæ killed, 24 hours after removal from the oil, was 87 per cent. A film 15μ thick effected approximately the same kill in 5 minutes.

Films 5μ thick of two fresh samples of the proprietary larvicides (Larvicides A and B) had appreciably the same toxicity when larvæ were exposed to their action for 5 minutes. But with 10μ films and an exposure of 10 minutes the toxicity of Larvicide A was higher than that of B.

A minimum thickness of 15μ is of practical importance, because larvæ caught in such a film are unable to leave it.

The mortality of larvæ increased with rising temperatures. It is possible that with 5μ and 10μ films of Larvicide A the increase may be of the order of 5 per cent for each degree rise in temperature.

Exposure of films of mineral oils to the atmosphere for periods of 30 minutes and over, or fresh films to the action of wind or agitation of the water surface, lowered the toxicity possibly by the loss of some of the volatile elements.

Films of oil became viscous with age and lost their penetrative power. A high water temperature partly compensated for this depending on the age of the film.

In the field this loss of toxicity and penetrative power are important factors, as the same larvicide has to be used in many different situation.

In the following two articles the abstracts made by the Editor, *Journal of the Malaria Institute of India*, are given below :—

OBSERVATIONS UPON THE EPIDEMIOLOGY OF MALARIA IN CEYLON

Regional epidemics of varying intensity occur at intervals of approximately 4 to 6 years. The drying up of river beds as the result of defective rainfall with the consequent production of pools suitable for the breeding of *A. culicifacies*, the sole mosquito carrier of any importance in the island, favour the production of epidemics in the Wet and Intermediate Zones. In the Dry Zone, excessive rainfall leading to the formation of large numbers of surface pools favours a rise in malarial incidence. Floods play a part in the causation of epidemics in the Dry Zone, but not in the Wet and Intermediate Zones. Epidemics occur in the Wet and Intermediate Zones chiefly during the periods April to June and October to December, and in the Dry Zone from October to February.

The Wet Zone is regarded as healthy, but liable to regional epidemics: the Intermediate Zone is for the most part moderately to highly malarious and is also liable to epidemics: whilst in the Dry Zone conditions are largely hyperendemic, and it is not subject to the violent outbreaks which are prone to occur in the other two regions.

The high spleen rates recorded throughout the island in 1936 represent the effects of the great regional epidemic of 1934-35. In the Dry Zone provinces the rates have continued at a high level, whilst in the Intermediate and Wet Zones the figures, after responding to the epidemics of 1934 and 1939, began to recede towards their former level after a lapse of 1 or 2 years.

Notable features regarding the parasite rates were their rapid regression to a low level when the epidemics subsided, the low figures recorded in the hyperendemic zone during the months of February and March, and the independent behaviour of parasite rates in relation to spleen rates in certain areas at varying periods.

P. vivax and *P. falciparum* are equally prevalent in the Wet Zone. *P. falciparum* is the more frequently encountered in the Intermediate Zone, whilst

P. malariae is the predominant parasite in the Dry Zone.

Death rates and birth rates return to normal within 2 years following a major epidemic, and infantile mortality rates do so within one year. Every rise recorded in the incidence of deaths from puerperal convulsions, has been shown to be the effect of malarial outbreaks.

In spite of intensive study of the various factors involved, no method of forecasting malaria epidemics in Ceylon with any degree of precision has as yet been evolved.

MALARIA IN THE JHARIA MINING SETTLEMENT, BIHAR. PARTS II, III AND IV

These parts give an account of investigations carried out up to 1943 on the local anopheline fauna, epidemiology of malaria and the effect of control measures adopted.

As the result of over 13,000 mosquito dissections, *A. fluviatilis* has been incriminated as the principal carrier of malaria. *A. stephensi* is rated as a vector of secondary importance, whilst *A. annularis* appears to be the sole carrier in the south-eastern corner of the settlement, where the physical features approximate those obtaining in deltaic Bengal. *A. pallidus* and *A. culicifacies* appear to be relatively unimportant, though chance infections of both these species have been encountered in localities where they are particularly abundant.

Adults of *A. fluviatilis* have been found almost exclusively in human dwellings, *A. stephensi* and *A. pallidus* in about equal numbers in human dwellings and in cattlesheds, whilst *A. annularis* and *A. culicifacies* appear to prefer cattlesheds as daytime resting places.

Seasonal malaria epidemics occur during the monsoon period (July to October). As a result of over 10,000 blood examinations, *P. falciparum* has proved to be the most prevalent parasite (54 per cent) as compared with *P. vivax* (35 per cent) and *P. malariae* (6.8 per cent).

The control measures adopted are claimed to have resulted in a considerable reduction of the malaria rate in those collieries where they have been carried out.

It has been observed that the period of minimum larval output of all the five species of mosquito in which natural infections of malaria have been encountered coincides with the height of the malaria transmission season. This is held to indicate that anti-adult measures are most likely to be effective at this period, whilst particular attention should be concentrated on antilarval measures before, and if necessary after, the peak period of transmission.

Reviews

MINOR SURGERY.—Edited by Sir Humphry Rolleston, B.T., G.C.V.O., K.C.B., M.D., F.R.C.P., and Alan Moncrieff, M.D., F.R.C.P. Publishers: Eyre and Spottiswoode (Publishers) Ltd., London. 1943. Price, 16s. net.

This handbook belongs to the series of the 'Practitioner handbooks' brought out by these distinguished editors. It contains 18 chapters on the following topics written by reputed authorities: Minor wounds, sprains, the feet, the hand, the mouth, the nose and throat, the ear, the eye, bursæ and ganglia, some benign tumours and cysts, skin infections, the rectum, the genito-urinary system, non-operative treatment of hernia, varicose veins and phlebitis, gynaecology, childhood, anaesthesia and analgesia. Each chapter is roughly 8 pages and provides a valuable and authoritative guide.

This is not a book on surgical handicraft, such as dressers in surgical wards possess. But the whole subject of minor surgery, including the specialties, is adequately covered as regards general principles. Although the treatment of some conditions is dealt with in detail, considerable attention is given to aetiology and pathology and to methods of prevention. The treatment of fractures and certain details of treatment, *e.g.* those concerned with the injection of varicose veins, etc., which have been included in other booklets of the series are not dealt with here. There are also 30 useful illustrations. The book may be a useful guide to the general practitioner and the hospital resident.

R. N. C.

MASS MINIATURE RADIOGRAPHY OF CIVILIANS FOR THE DETECTION OF PULMONARY TUBERCULOSIS. (London: H. M. Stationery Office. Price, 3s. net.)

SINCE the outbreak of war, miniature radiography of the chest on a large scale has made great strides both in Britain and in the U.S.A. for detection of symptomless or latent pulmonary tuberculosis, but most of the work of this type was at first confined to the services. In 1941, in view of the increasing incidence of tuberculosis in war time, the Medical Research Council appointed a committee of enquiry, and next year this committee issued a report, one of its proposals being for the controlled use of mass radiography among the civilian population. There was also a recommendation for the conduct of a survey for research purposes on a few selected civilian population groups, and the result of these investigations is embodied in the present report which is divided into two parts. Part I is a guide to the administration and technique of civilian mass radiography, accompanied by a good many illustrations. Part II contains the statistical results of the survey which covered over 23,000 persons, male and female, the examinations being entirely voluntary.

The incidence of tuberculosis in these persons as revealed by radiography, the bacteriological results of the survey, the symptoms of the patients who were found out and their bearing on the value of the method, and the associated problems are discussed. The report is a valuable one, and obviously much time and care have been spent by its authors not only in establishing standard methods and procedures, but also in exhaustive analyses of the information obtained.

R. N. C.

SYNOPSIS OF MEDICINE.—By Sir Henry Tidy. Eighth Edition. 1945. John Wright and Sons, Limited, Bristol. Pp. xx plus 1215. Price, 30s.

IN SPITE of war-time difficulties this edition has come out with numerous changes in the text, thus bringing it up to date and at the same time keeping its usefulness to both students and practitioners for revision as well as for reference. Recent advances in treatment have been included, but not the penicillin therapy, for, as the author explains in the preface, 'knowledge of its action is still advancing rapidly, and it has been considered wiser to omit such incomplete and ephemeral references as would alone have been possible at the time of revision'. We wish to make one or two comments. Thymol is hardly now used in the treatment of ankylostomiasis while much more effective therapy than x-rays and CO₂ snow is available for oriental sore.

R. N. C.

RECENT ADVANCES IN THERAPEUTICS (PARTS I AND II).—By J. R. Goyal, M.B., B.S. Second Edition. 1944. Pp. 346. Published by the author from Mission Church Road, Delhi. Price, Rs. 6-8-0.

THE first edition of this useful handbook was published in 1941 and was reviewed in this journal. Some of the suggestions given in our review of that edition have been incorporated in this edition. Moreover, this

edition incorporates the advances made in the subject since then and the subject is dealt with more elaborately and extensively than before, in spite of paper difficulties.

A TEXTBOOK ON DIETETICS.—By L. S. P. Davidson, B.A. (Cantab.), M.D. (Edin.), F.R.C.P. (Edin. and Lond.), F.R.S.E., and I. A. Anderson, M.B., Ch.B. (Aberd.). Hamish Hamilton Medical Books, London. Pp. xviii plus 324. Price, 10s. 6d.

THIS is a very practical book, and is strongly recommended to practitioners to whom nowadays a book on dietetics is a necessity. The work is divided into five parts; the first portion deals with the principles of nutrition based on recent experimental and clinical studies and stated in clear and concise language. The next section deals with the problems of diet in childhood, in pregnancy and lactation and in athletic training; and it also includes a chapter on diet in war time. The larger section of the book gives a full account of the dietetic treatment of various diseases with appropriate, though brief, references to other therapeutic measures as well. In the last part of the book are given tables, recipes and diet sheets which include many duplicates designed to meet the needs of both poor and well-to-do patients. The authors give only established facts that are of practical importance in the choice of diet in both health and disease, and we feel sure that the practitioners will find the book a reliable guide in dietetic treatment.

R. N. C.

BROMPTON HOSPITAL REPORT, VOL. XII, 1943

SIX out of the thirteen papers in this volume are on subjects connected with tuberculosis. Margaret Macpherson records the team-research work on childhood infection and its relation to adolescent and adult pulmonary tuberculosis, carried out in the hospital during the last fourteen years. The operation of extrafascial apicectomy with thoracoplasty is described in a long article by C. Price Thomas and W. P. Cleland; it is claimed that this at present is the best method for closing apical pulmonary cavities for which simpler forms of relaxation therapy are not applicable or have failed. In the next paper, the same authors report the results of thoracoplasty in a series of 120 cases. For tuberculous empyema, R. C. Brock advocates thoracoplasty unless there is an immediate response to conservative measures such as aspiration and lavage. W. D. W. Brooks discusses the place of miniature radiography in the diagnosis of diseases of the chest, quoting extensively from the Royal Navy figures to show the incidence of pulmonary tuberculosis as well as non-tuberculous intrathoracic disorders, while R. C. Wingfield has an article on the control of tuberculous infection. Then there are papers on traumatic hæmothorax (A. Tudor Edwards), on the use of silver nitrate in the production of aseptic obliterative pleuritis (R. C. Brock) and on a study of the bronchi (A. F. Foster-Carter) which is a sequel to a previously published paper on the same subject. Next we come to a subject of more general interest, *viz.* the health of the doctor, in which A. Hope Gose discusses the causes of ill-health and death among doctors. Finally, there are three articles on interesting cases—(1) a rare tumour of the lungs—'alveolar cell' tumour (Clifford Hoyle and J. V. Dacie) with symptoms like those of disseminated focal bronchopneumonia. (2) 'A case of hæmoptysis' (Clifford Hoyle and N. R. Barrett) in a girl of 17, in whom full investigations revealed nothing beyond some opacity in the upper part of the right lung which was however not of the type or extent to account satisfactorily for symptoms. As the bleeding was assuming alarming proportions, the upper and middle lobes of the lung were removed, but it still continued. The diagnosis, however, now became clear, and the source of the blood was traced to a place outside the lung. (3) In this case (Maurice Davidson, R. C. Brock and Standly Marshall), the prominent symptoms were

cough, sputum and hæmoptysis. The diagnosis suggested was either chronic abscess or else new growth, probably carcinoma, and the right lung was removed at operation. The autopsy findings are discussed and comment is made on the difficulties that may be experienced in such cases.

R. N. C.

MEDICAL RESEARCH COUNCIL, INDUSTRIAL HEALTH RESEARCH BOARD. REPORT NO. 86. A STUDY OF CERTIFIED SICKNESS ABSENCE AMONG WOMEN IN INDUSTRY.—By S. Wyatt. His Majesty's Stationery Office, London. 1945. Price, 9d.

ONE of the causes of decreased production in a factory is the absence of its workers due to sickness. There is a tendency to regard such absence as unavoidable, but a proportion of it can be reduced as shown by the facts that it is much lower in some factories than in others doing the same kind of work, that it varies with the hours and conditions of work, and that it is usually reduced by efficient medical and welfare services. The problem is, of course, also related to the wide background of diet, housing, transport, leisure and other specific factors. Before any steps can, however, be taken to reduce absence due to sickness, it is necessary to have accurate information on the amount, nature and causes of this type of absence, but this is by no means an easy task. An enquiry was therefore started by the Industrial Health Research Board of the Medical Research Council, its scope being limited to certified sickness of two or more days among women in factories where the records were reasonably accurate and complete. The result of this investigation is given in the present report which is based on a statistical study of the records of about 20,000 women employed in five munition factories during the last 6 months of 1942. The sickness absence in this group amounted to 7.8 per cent of the total number of days in this period, the respiratory, digestive and functional nervous disorders being the predominant causes. Married women, age groups of 30 to 50 and 'productive' workers had more absences, while those with clerical duties had the least. The percentage of women who had no sickness absence during the period was 45.3. Although the results of this investigation do not give us a complete picture of the causes of sickness absence in industry, they illustrate the importance of keeping accurate sickness records and the value of such records as an index of industrial health and also as an aid to the study of industrial diseases.

MEDICAL RESEARCH COUNCIL, INDUSTRIAL HEALTH RESEARCH BOARD. REPORT NO. 87. THE RELATION BETWEEN ILLUMINATION AND VISUAL EFFICIENCY—THE EFFECT OF BRIGHTNESS CONTRAST.—By H. C. Weston. Pp. 35. Published by His Majesty's Stationery Office, London. 1945. Price, 9d. net.

FACILITY with which objects can be seen depends upon certain characteristics such as their size, contrast and brightness, and upon the degree of illumination they receive. A. W. Beutell had suggested a method for determining the degree of illumination required for the efficient performance of any kind of work involving visual discrimination, and is based on the proposition that if the relationship could be ascertained between these characteristics for satisfactory visibility, then the illumination suitable for the performance ought to be capable of computation. The first report describing the relationship between illumination and size of object, was published some years ago. The present one describes two investigations to test the value of Beutell's method and deals with the relationship between illumination and the contrast of brightness.

R. N. C.

Abstracts from Reports

LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE. REPORT FOR 1943-44

It is now five years since normal teaching and research of the School came to an end; yet, despite war-time difficulties, it is gratifying to note that a good deal of useful work was done during the year, for which Professor Greenwood, the acting Dean, deserves credit, as he had to manage with many members of the staff absent on war service.

Seven special courses on tropical medicine and parasitology were held, which were attended by nearly 500 service medical officers. In addition, special courses including two week-end courses in industrial health were arranged. It was however not possible to conduct any clinical instruction on tropical medicine in hospital as beds had to be kept clear for air-raid casualties.

Dr. Buckley completed his work on onchocerciasis in East Africa while Dr. David concluded his researches on fumigants for lice; this work has now been published. Work with DDT has been carried out by several workers. Dr. Bracy is engaged in formulating a mosquito spray containing DDT. Mr. Musgrave has developed the impregnation of clothing with it as a measure of protection against the louse. The remarkable thing is that such clothing continues to kill lice in spite of being washed repeatedly.

Other activities included studies on penicillin, statistical work for several M.R.C. committees and research on industrial physiology. The branches of the Ross Institute in India and Ceylon have continued their anti-malarial work during the year as far as permitted by war conditions. The Institute of Agricultural Parasitology with Professor R. T. Leiper as its director, has been occupied during the year mainly with problems of helminth disease in plants of economic importance.

An outstanding event of the year was the election of Professor J. M. Mackintosh to the University Chair of Public Health *vice* Sir William Jameson. Professor Ryle and Professor Parry were appointed to fill two vacancies on the Board of Management. There are several vacancies in the School which are expected to be filled in near future.

THE SALVATION ARMY EMERY HOSPITAL AND TUBERCULOSIS HOSPITAL, 1943-44

THIS is an interesting report. Instead of being loaded with a mass of statistics, as is usual in reports of this kind, it says something about the influence of ignorance and poverty on patients and how these add to the doctor's difficulties in handling them. An eye may be lost if immediate action is not taken, but the patient postpones it, as there is a wedding in the family. A little baby is brought with dysentery; the doctor pleads with the parents to admit it. 'No, it is only teething. If we stay, who will look after the buffalo?' Blindness in young children is not uncommon, as owing to increased prices they are unable to get food containing fat soluble vitamins. There is an ever-increasing readiness to submit to operation; the surgical obsessions of the 'west', tonsils and appendix, have invaded India, and the diagnosis is frequently announced by the patient beforehand.

Patients come from long distances, and the number of outpatients may vary from 250 to 500. The hospital has 156 beds, but the average inpatient accommodation rarely falls below 200. There are 6 doctors, 13 trained nurses and 38 student nurses. A second operation theatre and a children's ward have been constructed, and additions made to the nurses' home and private rooms. The hospital is certainly popular, and the management is lucky in having the help of disinterested workers like Mr. B. H. Patel who collected

Rs. 18,306 from his friends, and Khan Bahadur K. A. Malek who presented an ambulance car. The report contains short clinical notes on sprue, pellagra and tropical macrocytic anaemia.

The tuberculosis hospital with three wards of 12 beds in each and five private rooms was opened in 1941. It is always full. Tuberculosis is said to be the 'most malignant disease in Gujarat'.

Correspondence

GUINEA-PIG INOCULATION IN THE DIAGNOSIS OF TUBERCULOSIS

SIR,—In his paper C. B. Dhurandhar (*Indian Journ. Med. Res.*, 29, 3rd July, 1941) has detailed a very useful piece of work, and the attention of many has been drawn to it. Should the suggestion in the paper by Dhurandhar be accepted the outlook of the diagnostic method is bound to change.

In fact many laboratory workers will recollect a circular asking for results of guinea-pig inoculation in their respective laboratories. From my laboratory, prior to 1942, I could find no positive result of inoculation recorded. The number of examinations were far too few, extending over many years, and no record of the method adopted and the accurate detail of technique, nor the clinical picture is available. I took up this question soon after receipt of the circular. The type of case selected was the one with persistent pleural effusion and the method adopted was briefly as follows:

Three c.c.m. of 3 per cent citrate in saline was put up in 2 ounce McCartney bottles. The bottles were sterilized. Fluid was directly received into the bottle. When material was sufficient, part of it was used for direct examination; there was no positive result. Depending on the dilution, 5 to 7.5 c.c.m. was injected intraperitoneally into guinea-pigs. A preliminary set of animals used to find out the suitable period showed that infection failed to occur at the end of 4 weeks. Number of the tests has been six, the control animals showing positive infection at the end of 6 weeks. The results are that out of 8 cases, 6 were positive and 2 negative. I have been unable to do parallel culture.

In November 1944 I happened to mention this at a meeting of teaching pathologists in Bombay. As a result of the discussion I undertook to inoculate guinea-pigs with known number of organisms from a strain kindly lent by Professor R. G. Dhayagude of the G. S. College. The culture was emulsified, and the emulsion in concentration of 1,000 organisms per c.c.m. was prepared. Animals were inoculated with 1 c.c.m., $\frac{1}{2}$ c.c.m., $\frac{1}{4}$ c.c.m., i.e. the number of organisms being 1,000, 500, 250, respectively. All animals showed tubercles in the spleen at the end of 8 weeks. The lesions were scraped and tubercle bacilli demonstrated.

My experiments have been few, yet the results are encouraging enough to warrant a re-examination of this problem. Dhurandhar has used the subcutaneous route throughout his investigations. I am inclined to think that the intraperitoneal route is the better one. I am not in a position to comment on the question of susceptibility or otherwise of different strains of guinea-pigs.

P. V. GHARPURE,
MAJOR, I.M.S./I.A.M.C.

DISTRICT LABORATORY,
BOMBAY.

HYPODERMIC SOLUTION OF SULPHATE OF QUININE

SIR,—I think the following abstract from *The Madras Monthly Journal of Medical Science* of June 1872, page 420, will prove that the use of quinine sulphate for preparing hypodermic solutions is really much older than most of us imagine:—

'On hypodermic solution of sulphate of quinine.—By Assistant Apothecary William Hamilton, acting assistant to the professor of chemistry, Madras Medical College.'

The following are the proportions which yield a solution suitable for hypodermic injection—

Quinia sulphate	10 grains
Diluted hydrochloric acid	8.5 minims
Water	10 minims

K. A. SHAH.

RANCHHODLAL DISPENSARY,
AHMEDABAD,
6th May, 1945.

Service Notes

APPOINTMENTS AND TRANSFERS

LIEUTENANT-COLONEL A. K. SAHIBZADA, O.B.E., Assistant Director-General, Indian Medical Service (Recruitment), is appointed to officiate as Deputy Director-General, Indian Medical Service, with effect from the 27th December, 1944, *vice* Colonel S. L. Bhatia, M.C., I.M.S., deputed *ex-India*.

Major H. B. Wright, Deputy Assistant Director-General (M.S.), Medical Store Depot, Calcutta, is transferred as Deputy Assistant Director-General (M.S.), Medical Store Depot, Madras, with effect from the afternoon of 22nd March, 1945.

Major W. T. Taylor, Deputy Assistant Director-General (M.S.), Medical Store Depot, Madras, is transferred as Deputy Assistant Director-General (M.S.), Medical Store Depot, Bombay, with effect from the afternoon of the 6th April, 1945.

Captain D. H. Harrison, an officiating Agency Surgeon, is posted as Civil Surgeon, Zhob/Loralai, with effect from the forenoon of the 27th February, 1945.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

To be Captains

J. L. Jogota. Dated 19th December, 1944.

S. Ghosh. Dated 20th January, 1945.

Alfred Saldanha. Dated 2nd February, 1945.

To be Lieutenants

3rd April, 1943

A. J. E. Bradfield.

S. H. Barker.

Arsene Lazare.

D. M. Gomez.

Robert Henry Baker. Dated 25th July, 1944.

Satyendra Singh. Dated 16th September, 1944.

Gora Chand Dhar. Dated 7th November, 1944.

16th January, 1945

Basil William John Ince.

Desmond Andrew William Nugent.

17th January, 1945

H. L. Dutta.

Mahalingamoorthy Natarajan.

Govindappa Venkataswamy.

19th January, 1945

G. D. Dhavle.

Ramamritham Tyagarajan.

Mohamed Abdul Jameel.

Durai Raja Ayyar Lakshmanan.

Lakshman Sathyavageesswaran.

Gopala Kuppaswamy.

20th January, 1945

Shermadevi Palvannasundara Subramanian.

Varadarajulu Nandaraman.

Ulaganatha Sankaranarayanan.

Kochat Purushothaman.

S. S. Dighe. Dated 21st January, 1945.
 Arepally Sri Ramamoorthy. Dated 21st January, 1945.
 Peter Ian Atkinson. Dated 19th February, 1945.

INDIAN MEDICAL SERVICE—SECONDED TO THE INDIAN
 ARMY MEDICAL CORPS
 (Emergency Commissions)
 (WOMEN'S BRANCH)
 To be Lieutenants

(Miss) Saraswati Mitra. Dated 1st February, 1945.
 The undermentioned officers of the Indian Medical
 Service (Emergency Commission) revert from Indian
 Army Medical Corps and are seconded for service with
 the Royal Indian Naval Volunteer Reserve:—

9th March, 1945
 Lieutenant Ch. Mohd. Anwar.
 Lieutenant K. S. Isar.
 Lieutenant K. A. Malik.
 Lieutenant P. C. Bhoil.
 Lieutenant M. P. Bhalla.
 Lieutenant A. Nazami.
 Lieutenant A. Jayachandra.

PROMOTIONS

The undermentioned Indian Medical Service Officer
 is advanced to the list of special selected Lieutenant-
 Colonels:—

Lieutenant-Colonel A. S. Fry, C.I.E. Dated 25th
 August, 1944.

INDIAN MEDICAL SERVICE
 Captain to be Major

D. P. Nath. Dated 21st November, 1939.

LAND FORCES—INDIAN MEDICAL SERVICE
 SECONDED TO THE INDIAN ARMY MEDICAL CORPS
 (Emergency Commission)
 Captains to be Majors

V. P. Patel. Dated 1st September, 1944.
 D. J. Shroff. Dated 1st February, 1945.
 O. J. S. Macdonald. Dated 6th February, 1945.
 W. G. Aranha. Dated 14th February, 1945.
 R. Rajagopalan. Dated 26th February, 1945.

1st March, 1945

P. G. Rau. J. R. Sen.
 S. L. Rikhye.

M. K. K. Menon. Dated 3rd March, 1945.
 V. R. Kamath. Dated 10th March, 1945.
 T. K. Narayanan. Dated 15th March, 1945.
 S. C. Ray. Dated 29th March, 1945.

Lieutenants to be Captains

S. Singh. Dated 7th December, 1944.
 J. Chandra. Dated 14th March, 1945.

15th March, 1945

A. K. Basu. S. K. Basu.
 S. C. Sarkhel.

R. B. Rawat. Dated 16th March, 1945.
 24th March, 1945

G. Crosse. G. F. Perry.
 (General Service)

Balakrishna Nair. Dated 3rd October, 1943.
 S. S. Grewal. Dated 28th February, 1944.
 B. B. Sarkar. Dated 21st April, 1944.
 J. N. Dutta. Dated 16th July, 1944.

19th October, 1944

U. N. Chakraborty. R. G. Thadani.
 M. L. Ghate. Dated 11th January, 1945.

(WITHIN INDIAN LIMITS)

3rd April, 1944

A. J. E. Brafield. S. H. Barker.
 D. M. Gomez.

Sant Singh. Dated 11th January, 1945.

INDIAN MEDICAL SERVICE—SECONDED TO THE INDIAN
 ARMY MEDICAL CORPS
 (Emergency Commission)
 (WOMEN'S BRANCH)
 Lieutenants to be Captains

16th October, 1943

(Miss) G. E. L. Cummins.
 (Mrs.) M. S. Austin (Nee Garden).

(Miss) A. Dowds. Dated 15th January, 1944.
 (Miss) R. S. McGowan. Dated 14th February, 1944.
 (Miss) D. J. Ball. Dated 1st June, 1944.

15th August, 1944

(Mrs.) S. M. L. Howell Roberts.
 (Miss) R. L. McCully.

21st September, 1944

(Miss) C. T. Howat. (Miss) F. G. Danson.

RETIREMENT

Lieutenant-Colonel S. L. Patney. Dated 8th Feb-
 ruary, 1945.

RELINQUISHMENTS

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
 SECONDED TO THE INDIAN ARMY MEDICAL CORPS
 (Emergency Commissions)

Captain George Henry Durairaj, on grounds of ill
 health, and is granted the honorary rank of Captain.
 Dated 11th February, 1945.

Captain Pispati Venkatnarayan, 24th February, 1945,
 on grounds of ill health, and is granted the honorary
 rank of Captain.

Captain A. Babu Rau, on grounds of ill health, 2nd
 March, 1945, and is granted the honorary rank of
 Captain.

Captain Mohamed Amin, 6th March, 1945, on
 grounds of ill health, and is granted the honorary rank
 of Captain.

Major S. V. Velankar, on grounds of ill health, and
 is granted the honorary rank of Major. Dated 11th
 April, 1945.

Captain Muddassir Khan, on grounds of ill health,
 and is granted the honorary rank of Captain. Dated
 11th April, 1945.

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Original Articles.

UNCOMMON ETIOLOGICAL FACTORS IN PATHOLOGICAL CONDITIONS OF THE GALL-BLADDER

By V. M. KAIKINI, B.A., F.R.C.S. (Edin.)
King Edward Memorial Hospital, Bombay

THE majority of the pathological conditions of the gall-bladder are due to inflammation with or without the presence of stones in it. The inflammation in cholecystitis is intra-mural, and this fact has to be taken into consideration before a course of treatment is thought of. The presence of inflammation naturally means that infection by some organism has occurred. There are however cases where organisms have been detected in the bile or gall-bladder, but the viscus is found to be normal to all intents and purposes. For instance, many patients with cholecystitis (about 30 per cent in my experience) give a history of an attack of typhoid, but many of the so-called carriers of typhoid have been found to be completely free from any symptoms which point to the existence of any lesion in the gall-bladder. The general opinion is that for a pathological condition of the gall-bladder to occur, there must be a previous damage to the viscus, on the top of which there is a superimposition of infection by some specific organism.

The most common factors in causing damage to the gall-bladder are metabolic disturbances and biliary stasis. Of these two, stasis plays the more important rôle. In the majority of cases this is due to dysfunction of the vagus nerve or the inco-ordination between the vagus and the sympathetic, with disorganization of the duodenal reflex, resulting in obstruction to the flow of bile from the gall-bladder. Many of the symptoms, e.g. nausea, vomiting and distension, according to Zollinger, can be duplicated by the inflation of a balloon in the duodenum. So these symptoms in cholecystitis are due to interference with the normal motor functions of the pylorus and the duodenum produced by reflexes arising in an inflamed gall-bladder. The presence of acid chyme in the duodenum not only causes a relaxation of the sphincter of Oddi but stimulates evacuation of the gall-bladder. When the acid is absent (due to dysfunction of the vagus) and the gall-bladder is lacking in tone, the stimulus may be inadequate to produce evacuation, which results in disease of the viscus. This is the hypotonic type of gall-bladder. In the hypertonic type, the stimulation of the vagus may be due to duodenitis, appendicitis, spastic colon, pelvic diseases, pregnancy, etc.; and spasm of the sphincter of Oddi occurs followed by stasis of bile. The condition after some time damages the gall-bladder and prepares the ground

for inflammation by infective organisms. The stimulation of the vagus is not only caused by the above diseases but also by the habits of the patients, such as irregularity in meals. These are the commonest etiological factors in the causation of the pathological conditions of the gall-bladder but below are quoted some uncommon ones, congenital or otherwise, which were found amongst 115 cases operated on by me during the last few years.

Case 1. Papilloma of the gall-bladder.—Multiple papillomata usually occur on the mucous surface of the organ and the condition is supposed to be very rare. In my case the patient came complaining of pain in the right side of the abdomen for about four years. On opening the abdomen a small nodule, papillomatous in nature, was found on the fundus of the gall-bladder, which was removed and the patient felt better for some time. But the pain recurred and remained for nearly one year (post-cholecystectomy pain) and then it completely disappeared. There was no other abnormality and probably the papilloma was responsible for the original pain (figure 1, plate XII).

Case 2. An abnormal branch of the hepatic artery with a diseased gall-bladder.—Many varieties of abnormalities have been mentioned in the arteries supplying the gall-bladder and the liver. For example, according to J. Reginald Jackson, in 20 per cent of cases the blood supply of the right hepatic lobe comes directly from the superior mesenteric artery; and this hepatic branch may meander so far as to lie across the cystic duct. If mistakenly ligated, high temperature and death may follow. In some cases the right hepatic artery runs parallel to the cystic duct and then arches behind it at the neck of the gall-bladder to enter the right lobe of the liver. Before doing so it gives off the cystic artery. Many other abnormal courses of the cystic artery have also been noted. In the present case, the cystic artery arose as normally, but an abnormal branch of the right hepatic artery ran parallel to it, and, passing along the wall of the gall-bladder, terminated in the right lobe of the liver. The gall-bladder was very much atrophied with its walls fibrosed and thickened. The patient had been suffering from severe and persistent pain in the right hypochondriac area for about six years. It was impossible to set the artery free from the wall of the gall-bladder, as it was firmly adherent to it. It was ligated and cut, and the gall-bladder removed. The patient got completely rid of his symptoms and was in perfect health when seen about a year after the operation. Apparently the right lobe of the liver was not deprived of its blood supply by the ligation of the vessel as this must have been an accessory branch from the right hepatic artery (figure 2, plate XII).

Case 3. Congenital narrow lumen of the bile ducts.—A young man of about 25 years

came with a history of abdominal pain on the left side of the umbilicus, with belching, and also intermittent pain in the cardiac area. The trouble first started with pain in the cardiac area and then dyspeptic symptoms appeared with loss of appetite. He had been treated in the Miraj Hospital with decholine and other drugs which only gave him temporary relief. Tenderness was present in the lower abdomen about $1\frac{1}{2}$ inch below and to the left of the umbilicus; it disappeared with pressure in the gall-bladder area which was also markedly tender. Cholecystography showed defective filling. At operation the gall-bladder was found to be free from adhesions and normal in appearance, but the cystic and common bile ducts were found to be extremely narrow. The gall-bladder was removed. The patient developed slight jaundice on the fourth day after the operation, but it disappeared on the sixth day. Perhaps, it was due to the temporary obstruction of the lumen of the common bile duct on account of the oedema of the mucous membrane caused by handling during the operation. The pain in the cardiac area soon disappeared completely, and the dyspeptic symptoms and the abdominal distress went on improving gradually. When seen three years later, he was feeling very much better and stronger, and his appetite had improved. In this case the whole trouble was probably due to a congenital narrow lumen of the bile ducts. According to Illingworth the lumen of the common bile duct has been found to increase in size after removal of the gall-bladder. In this case the gradual improvement must have been due to that factor.

Case 4. Incorporation of a part of the circumference of the wall of the fundus of the gall-bladder in the substance of the liver.—Normally, the gall-bladder is found lying on the surface of the liver fixed to it by the serous coat, and not buried in its substance. When it is removed, a flat raw area is left behind on the surface of the liver. In this case the patient was admitted for pain in the epigastrium and right hypochondrium. The appendix had been removed some time before with temporary relief. At present the attacks of pain were intermittent and spasmodic in character, with tenderness over the gall-bladder. On opening the abdomen the gall-bladder was found to be free from adhesions, and normal in colour and appearance, but it was rather small in size, lying parallel to the anterior margin of the liver and some portion of the circumference of the fundus was found lying buried in the substance of the liver. Perhaps, this congenital abnormality prevented the full play of the fundus during its rhythmical contraction and gave rise to spasm and caused the symptoms. The organ was not removed.

Case 5. A similar condition with superimposition of infection.—This gives rise to well-marked inflammatory changes in the gall-

bladder. A female patient was admitted for persistent and severe pain in the right hypochondriac region for the last four years with loss of appetite and debility. She had had an attack of typhoid about nine years previously. The gall-bladder was found to be atrophied, with the wall very much thickened and fibrosed, and the fundus firmly fixed to the duodenal wall by a thick broad fibrous band which had to be cut through to set it free. The viscus contained one big stone. The fundus was found to be buried to about half of its circumference in the substance of the liver, and had to be dissected out of its bed with the knife. Typhoid infection on the top of the congenital defect must have given rise to the inflammatory condition with formation of stone (figure 3, plate XII).

Case 6. Absence of a regular cystic duct, and the gall-bladder fundus opening directly into the common bile duct.—A patient about 55 years of age was admitted for jaundice and persistent abdominal pain of over six years' duration. Operation after disappearance of the jaundice revealed an enlarged, fibrosed and thickened gall-bladder with a portion of the fundus deeply buried in the liver substance, and the cystic duct practically absent. The fundus opened into the common bile duct by means of a broad channel. The whole viscus was covered with thick adhesions which were most marked over this channel. The latter was isolated and ligated, and the major portion of the fundus which contained three big stones was removed, but a small portion which was embedded in the liver substance and firmly fixed was left behind. It ought to have been removed along with the adherent portion of the liver substance. Perhaps, the leaving behind of a portion of the wall of a very septic gall-bladder gave rise to pyelophlebitis, and the patient died of jaundice on the twelfth day after the operation. This type of abnormality has been described by Jackson (1938). On account of the fundus being partly buried in the liver substance, there was an impediment to its rhythmical contraction, and the flow of bile to and from the gall-bladder was not well regulated on account of the absence of a regular cystic duct equipped with valves (figure 4, plate XII).

Case 7. Ptosis of an elongated and atonic gall-bladder with a long and narrow cystic duct.—The patient was admitted for severe pain in the epigastric region, and vomiting. About 18 months before he had similar pain with hæmatemesis, and had gastro-jejunostomy done in another hospital as for duodenal ulcer. He felt perfectly well for about three months; but after that, severe abdominal pain with vomiting again started. He was a heavy smoker and took alcohol rather freely. He was admitted as a case of suspected jejunal ulcer, but this was excluded on radiological examination. The pain complained of was intermittent,

and of a very severe nature; and the tenderness in the gall-bladder area was most marked during the attack of pain. Westphal's syndrome was very marked, but in the interval between pains it was practically absent. On opening the abdomen the gall-bladder was found enlarged, with some adhesions, and lying rather low down, and the cystic duct was narrow and elongated. The gall-bladder was removed and the patient has since been completely free from symptoms. In this case the intermittent attacks of severe pain were probably due to spasmodic contractions of the cystic duct aggravated by the low-lying position of the gall-bladder. The absence of tenderness and of the Westphal's syndrome in the intervals between the attacks of pain is significant, showing that the inflammatory condition was not severe.

As regards diagnosis by x-ray: no doubt when radio-opaque stones are present in the gall-bladder x-ray diagnosis is very useful; but when stones are present, the value of x-rays in diagnosis is often doubtful. Says Kunath (1937): 'A disturbing factor is the relatively high percentage of cures in the group of patients with normal or nearly normal gall-bladders. Many patients got relief of symptoms after removal of a gall-bladder showing very little pathological change. 73 per cent of patients with normal cholecystograms were cured by operation. Cholecystography cannot be relied upon either for diagnosis or for prognostic purposes following cholecystectomy, but pre-operative symptoms are of great value.' One comes across a fair number of cases where not only are the symptoms atypical but cholecystography is of little value in diagnosis.

Case 8. I was called in to see a patient in 1925 with severe 'heart attack.' I suspected it to be a case of biliary colic from the way the patient was shouting and his body was contorted. He improved a little with treatment designed for biliary trouble; the case could not be followed till 1935. During this interval he was being treated for suspected heart and kidney troubles. Now he was very much debilitated and had a slight icteroid tinge in the conjunctiva and severe abdominal pain. Cholecystography revealed a normally functioning gall-bladder. Removal of the gall-bladder completely cured the patient. Two things are of significance in this case. The first is the diagnosis of heart disease. When seen during the first attack of pain, he persistently pointed to the cardiac area as the site where the pain was most severe, but colic was suspected. When asked about the radiation of pain, he pointed toward the epigastrium and left shoulder. When the abdomen was palpated, the gall-bladder area was found to be very tender. This made me suspect biliary colic. Secondly, the cholecystogram showed a normally-filling gall-bladder. On opening the abdomen it was found to be slightly enlarged

and covered with adhesions. Cholecystectomy completely cured the patient, and at present he is enjoying perfect health.

In some cases of cholecystitis, patients complain of pain more on the left side. In one such case the pain was of a severe colicky type, had been increasing for about four years and was in the left hypochondrium, but there was no pain in the right side although the gall-bladder was definitely tender. After its removal, the patient continued to complain of the pain, though less severe than before, for a few months longer, and then it disappeared completely. In about 30 per cent of cases I have found the patients complaining of pain and tenderness at a spot $1\frac{1}{2}$ inch to the left and below the umbilicus. In two cases of advanced cholecystitis (one with stones but no jaundice, and another without stones but slight jaundice) this was the only site where the pain was complained of, although well-marked tenderness was found over the gall-bladder. Both these were completely cured of their trouble after cholecystectomy. It is rather interesting to note here that the patient without stones (an educated man) gave a history of occasional hæmaturia although the skiagram did not reveal any stones in the kidney. According to Charles Mixter, 'Left-sided pain in biliary-tract disease is usually explained by pancreatitis, or extension of pericholecystitis to the left side without extension of the inflammatory process. On embryological grounds the common duct must be assumed to have a bilateral innervation. This would explain the occurrence of left-sided pain.' The occurrence of hæmaturia in the above case might have been due to a tendency to hæmorrhage on account of the presence of jaundice for some months.

Case 9. *The presence of a gall-bladder stone along with a stone in the kidney.*—The patient was admitted for a very severe attack of acute cholecystitis with well-marked jaundice, pain and fever. X-ray showed the presence of two stones round about the gall-bladder, but at the operation only one stone was found in it. The common bile duct was opened and explored but no stone could be detected in it. Cholecystectomy was done and the patient was discharged free from all symptoms. Radiogram after the operation showed the second stone lying stationary in its original place. Obviously it was a kidney stone although the patient who has been keeping very good health since the operation has never complained of any symptoms referring to the kidney (figure 5, plate XII).

Case 10. *Cardiac lesion due to an old pathological condition of the gall-bladder.*—Male patient aged about 46 had a severe attack of 'palpitation of the heart' with other symptoms of 'angina' in 1930. The attack was accompanied by distension of stomach and flatulence. Well-regulated diet and sedatives improved his

condition although he used to complain frequently of heaviness in the cardiac area and flatulent dyspepsia. A similar but milder attack occurred in 1942; but this time the symptoms of gastric distress were more marked. Treatment was given on similar lines and the condition improved. I however suspected that the gall-bladder was the original cause of the trouble, as it was very tender. The physician-in-charge agreed with me, and on radiological examination it was found to be badly functioning. The electro-cardiogram showed a slight left axis deviation. In this case the most likely primary cause was a pathological gall-bladder and this must have caused some secondary degeneration of the heart muscle.

There seems to be a very close connection between the pathological condition of the gall-bladder and the heart. According to Laird, thrombosis of coronary arteries occurred in 12 per cent of cholecystitis cases, and cholecystectomy cured 78 per cent of 'heart cases' with gall-bladder symptoms. He is of opinion that gall-bladder disease is a definite etiological factor in myocardial lesions; it produces abnormal T wave changes in the electro-cardiogram which disappear after removal of the diseased organ. The incidence of atheroma of the arteries has been found to be high in people with cholecystitis.

Post-cholecystectomy pain is one of the things that causes worry to the patient and also to the surgeon. Usually it remains for about a month or two, although mild in nature. It is usually due to disturbance in the adjustment of the abdominal nervous system caused by the removal of an important organ. In most cases it disappears with a mixture containing a vago-sedative such as belladonna and some alkalis. In some nervous people the pain continues for some months. In two cases small doses of insulin, 10 units daily for about a week, completely cured the patients. One of the causes of persistent pain is supposed to be post-operative adhesions between the duodenum and

the raw area left behind on the surface of the liver after removal of the gall-bladder. This can be prevented by covering the raw area with the serous coat dissected off the gall-bladder, but where this is impracticable, the great omentum should be utilized.

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OCCURRENCE OF FLUOROSIS IN ENDEMIC FORMS IN HYDERABAD STATE*

By M. B. DAVER, M.B., B.S. (Bom.), F.R.F.P. & S.G., D.P.H. (Eng.)
Nutrition Officer, H. E. H. the Nizam's Dominions

ALL animal tissues and plants contain fluorine in very small amounts. It is found in soils, rocks and water.

No convincing evidence has been as yet produced to show that it performs any useful function in animal nutrition, or that it is essential for animal metabolism. During the past 15 years, however, evidence has been accumulated to show that the prolonged ingestion of abnormal quantities produces a chronic toxic state, the earliest visible sign of which is called 'mottled enamel' of the teeth or chronic dental fluorosis. Its most common source is drinking water, and the level above which effects are produced is about one part of a million, equivalent to $\frac{1}{16}$ grain of fluorine to a pint of water. However, it is interesting to note that increased immunity to dental caries is supposed to be associated with an increased intake of fluorine (Wilson, 1941).

The presence of fluorosis in the Madras presidency was investigated first in 1937 by Shortt and others. In 1940, Raghavachari and Venkataramanan recorded the wide distribution of fluorides in the water in the province, and they indicated the districts of Bellary, Kurnool and Guntur as an endemic area. These districts are separated from Raichur, Mahboobnagar and Nalgonda districts of Nizam's Dominion by the river Krishna. This led us to believe that those districts of our Dominion which were adjacent to the Madras presidency might have waters containing fluorine, and that we might find cases of chronic fluorine intoxication. Therefore, while doing nutrition and diet surveys of the districts, we took an opportunity to look for cases of fluorine intoxication and to determine the fluorine content of water used for drinking (see Map). In all these districts, well-water contained fluorine ranging from 0.25 part to 4 parts per million, and we came across children

EXPLANATION OF PLATE XII

Fig. 1.—Gall-bladder enlarged and having a small papillomatous growth at the fundus.

Fig. 2.—Gall-bladder is atrophied, coat is thickened and changed in colour. The aberrant artery is shown as a branch of the right hepatic artery going along the wall of the gall-bladder and entering the right lobe of the liver: (1) hepatic artery, (2) pylorus, (3) cystic duct, (4) pancreatic duct, (5) pancreas, (6) common bile duct, (7) aberrant branch of hepatic artery, (8) cystic artery, (9) liver.

Fig. 3.—Gall-bladder fibrosed and atrophied. The fundus is slightly buried in the substance of the liver and is firmly adherent to the wall of the duodenum.

Fig. 4.—An enlarged gall-bladder full of adhesions and directly communicating with the common bile duct without the regular cystic duct being present.

Fig. 5.—Skiagram shows two stones, one in the gall-bladder the other in the kidney.

* Paper presented before the Indian Science Congress Association, 32nd Annual Meeting, held at Nagpur, January 1945.

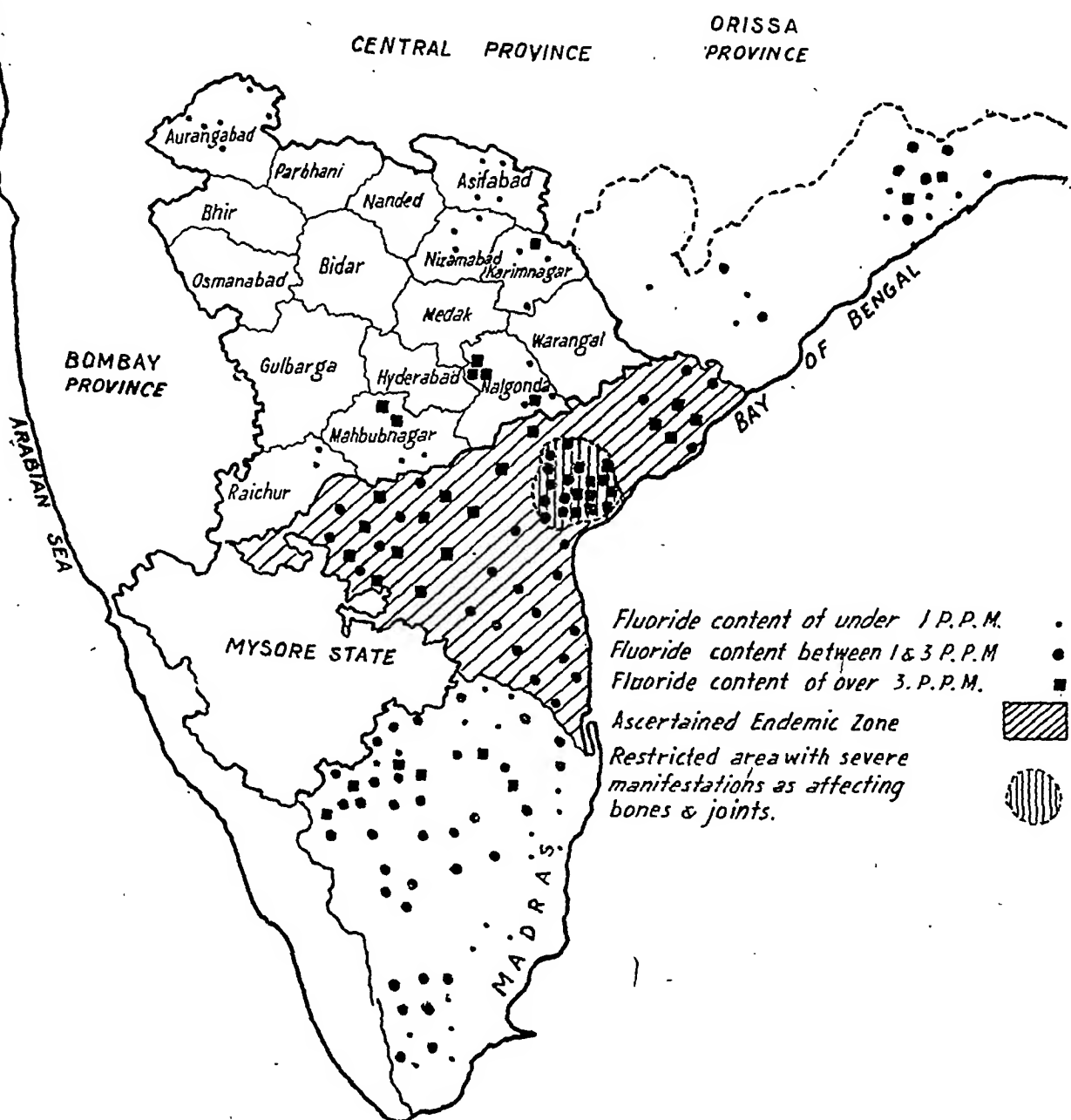
showing mottled enamel of the teeth. A good many cases of bone involvement and joint affections in elderly people were also seen clinically; unfortunately the diagnosis could not be confirmed by x-ray examination.

Table I shows the parts per million of fluoride content of water in different districts, with their geological strata. The water from

Before giving the results of the survey, it will be of interest to define the various appearances of the teeth in chronic fluorine poisoning.

In chronic fluorine intoxication, the teeth and bones suffer most. Mottled enamel is one of the first signs, the outer surface of the front teeth being most affected. Opaque, paper-white patches or horizontal or curved bands begin to

Map showing fluoride content of water in the different parts of Hyderabad and South India.



these wells is in actual daily use. These wells are mostly dug in rocky strata to a depth of 60 to 80 feet.

Examination of water from different districts showed that the occurrence of fluorine was widespread, and that water flowing over granitoid rocks invariably contained fluorides. These places, with their geological strata, have been shown in the accompanying Map.

appear. Sometimes the whole of the surface of the tooth becomes chalky-white in appearance. The tooth may remain chalky-white, or, later on brown, yellowish, or black marking may appear.

The process is very slow in appearing and in progressing. This sign appears during the period of calcification of the enamel of teeth, in those who reside in an area where the fluorine

content of water is well over the threshold level, that is, above one part per million. As the condition progresses, pits appear.

Histologically, it is said that there is a lack of cement substance between the enamel rods.

appears as age advances? This point needs further investigation.

The total number of children and adults examined between the ages of *four* and *twenty*, was 4,243. Out of these, 16 per cent showed

TABLE I

Fluoride content (in parts per million) of water in different districts, with their geological strata

Districts	Taluka	Name of village	Fluorine content of water source, in parts per million	Geological formation
Nalgonda	Jangaon Suryapet	Pangiri	Between 2 and 3	Granite
		Pankhad	Less 1	"
	Nalgonda	Yellareddyguda	Between 2 and 3	"
		Cherugutta	" 2 and 3	"
		Narkatpally	" 2 and 3	"
		Naryanpur	" 3 and 4	"
		Katangur	" 2 and 3	"
		Munikuntla	" 2 and 3	"
	Miryalguda	Damarcherla	" 2 and 3	Shales
		Settipalam	" 3 and 4	Granite
		Lachmapur	Less 1	"
Mahboobnagar	Amrabad	Mananur	Between 1 and 2	"
		Dharawaram	" 1 and 2	"
		Farhabad	" 1 and 2	Quartzite
	Nagarkurnool Kolapur (S)	Kolapur	" 1 and 2	Granite
		Yadreddipalli	Over 3	"
		Kopnoor	Between 2 and 3	Limestone
Raichur	Alampur	Bukkapur	Less 1	"
		Chinnapadu	Between 1 and 2	Shales
		Hundevalli	" 1 and 2	"
		Imampur	" 1 and 2	Limestone
		Manopadu	" 2 and 3	"
		Alampur	" 4 and 5	"

In severe cases, the enamel prisms are not well calcified.

The severity of the lesions increases with the concentration of fluorine in water and the length of time of its ingestion. Normally, there is no effect on general health, and in very mild cases there may be nothing more than some white spots. But there is some relation between the food intake and effects of fluorine intoxication, as its effects are enhanced in ill-nourished people, and decrease with better food, as will be shown later.

Chalkiness, staining and pitting of the enamel of teeth depend upon the concentration of fluorine in water and also upon the length of time of its ingestion. In our series, chalkiness of the enamel was found in those villages where fluorine concentration was between *one* and *two* parts per million, and mostly in children between the ages of *six* and *fourteen*. A concentration of *two* parts per million and over induces first deeply-stained and later on pitted enamel, mostly seen between the ages of *sixteen* and *twenty*. But it was surprising to find that these various changes in teeth were seen in persons up to the age of *thirty*; after this age these tooth manifestations were not seen, even though they were inhabitants of the place for more than forty years. Does this mean that this sign dis-

chalkiness of teeth and 21.7 per cent mottled and pitted enamel as shown in table II.

TABLE II

Manifestations of fluorosis between the ages of 4 and 20

Districts	Total number	Chalkiness	Mottling and pitting	Fluorine content of water source, in parts per million
Nalgonda ..	2,173	10.3%	3.2%	Between 1 and 2
Mahboobnagar ..	1,405	4.8%	4.0%	Between 2 and 3
Raichur ..	665	1.0%	14.5%	Above 3

4 During the routine survey at Yadreddipalli of the Mahboobnagar district, it was observed that the percentage of fluorine intoxication amongst the local population was higher, though fluorine concentration in water was only 1.5 parts per million, whereas the Christian settlers of the same village showed a lower incidence of fluorine intoxication though the water they consumed had a fluorine concentration above 2.5 parts per million. These Christian settlers had been staying in the village for more than two decades.

Socially and economically, the Christian settlers staying in the village were better off; this led us to believe that there would be a corresponding disparity in the state of their nutrition, and we carried out detailed surveys of these two groups.

Diet surveys of both the groups were carried out for seven consecutive days; and it was observed that cereals consumed by both the communities were the same in quantity. Vegetables were almost absent from both the diet schedules, but green chillies were consumed in very good amounts by both the groups. The Christian settlers however consumed larger quantities of pulses and small amounts of milk and its products, and oil and ghee, whereas the local population used them in almost negligible amounts.

per million, and the incidence of fluorine intoxication 10 per cent, whereas the fluorine content of water consumed by the local population was 1.5 parts per million, and yet the incidence of fluorine intoxication was 17 per cent. These facts suggest a relation between better food and lower incidence of chronic fluorine intoxication.

Summary

Chronic fluorine intoxication is present in Raichur, Mahboobnagar and Nalgonda, the districts adjacent to the Madras presidency. It is not localized to these districts only. Its incidence is widespread in the Dominion. Analysis of water for fluorine shows that the water which

TABLE III
Diet in ounces

	Home-pounded rice	Jawar	Italian millet	Pulses	Leafy vegetables	Non-leafy vegetables	Oil	Ghee	Milk	Buttermilk	Meat, eggs	Fruits	Condiments
Christian settlers	6.7	14.3	4.5	1.5	0.08	0.01	0.3	0.8	1.0	3.1	0.7	..	2
Local population	3.1	18.5	5.5	0.5	0.08	0.02	0.2	1.7	2

TABLE IV
The analysis of the above diets

	PROTEIN IN GRAMMES			FATS IN GRAMMES			Carbohydrates in grammes	Calcium in grammes	Phosphorus in grammes	Iron in grammes	Calories	VITAMINS		
	Animal	Vegetable	Total	Animal	Vegetable	Total						A (I.U.)	B (I.U.)	C (mgm.)
Christian settlers	9.1	81.2	96.3	21.2	20.4	41.6	592	0.45	1.9	45.4	3,067	1,035	601	62
Local population	0.7	73.7	74.4	1.0	18.8	19.8	542	0.32	2.08	43.1	2,635	705	272	53

It is seen from tables III and IV that the diet received by Christian settlers is decidedly better than that of the local population. The diet of the local population is very deficient in its fat, calcium and vitamin contents. Vitamin C in both diets appears to be adequate, but since investigations were carried out during winter, its adequacy was maintained by green chillies alone, as the amount of leafy and non-leafy vegetables taken is almost negligible. During other seasons, dry chillies take the place of green ones, and this would necessarily lower the vitamin C intake.

The fluorine content of water consumed by the Christian settlers was between 2 and 3 parts

flows over granitoid strata invariably contains fluorine.

A fluorine content of water less than one part per million appears to be innocuous; within this limit, it is supposed to prevent dental decay. Above this threshold, i.e. 1 part per million, it produces various manifestations of chronic fluorine intoxication, which chiefly affect the enamel of teeth and bones. The severity of the lesions increases with the concentration of fluorine in water and the length of time of ingestion.

The incidence and severity of the disease have some definite relation to the economic and nutritional status of the communities.

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LEPTOSPIROSIS WITHOUT JAUNDICE

By M. N. LAHIRI

(From the Haffkine Institute, Parel, Bombay)

THE cases of leptospirosis reported by the writer in previous communications (Lahiri, 1941, 1943) as well as those detected subsequently with the aid of laboratory studies all developed jaundice as an important symptom. Since the disease has been described in textbooks under different names, *i.e.* spirochætal jaundice or infective jaundice (Weil's disease), it is considered that the disease should always be associated with jaundice. It is now an established fact that many cases do not produce icterus at all. According to Schüffner (1934), in more than half of the cases studied in the Netherlands, this symptom was absent. Fletcher (1927) also did not note jaundice in some of his cases of leptospirosis in the Federated Malay States. Taylor and Goyle (1931) in their comprehensive investigation in the Andamans recorded that out of 64 cases observed in 22 there was a total absence of jaundice. In 16 of these cases, however, the diagnosis was confirmed by the demonstration of leptospiræ in blood or urine, and in the remaining 6 the diagnosis was based on clinical grounds alone. Thus, it appears that the clinical manifestation of jaundice in the diagnosis of this infection is perhaps not more important than the appearance of a rash in a case of enteric fever. The non-icteric form of the disease no doubt presents considerable difficulty in diagnosis without laboratory investigations. In the literature, cases without icterus so far have not been recorded in this country. It is obvious, therefore, that unless clinicians are on the lookout for the presence of this form of the disease, such cases will continue to pass unsuspected or will be incorrectly diagnosed. In view of the above fact an account of the following case seems worth reporting.

The patient, a well-built male, was admitted to the hospital for fever, headache and agonizing pains all over the body. He was seen on the eighth day of illness. The history suggested acute onset with rigors, and on examination the pain was noticed over the loins, and the tenderness over the calf muscles appeared to be so marked that with slight pressure the patient cried out with pain. The temperature recorded was 99.2°F. The conjunctivæ were intensely congested. Prostration to a moderate degree was present. Examination of the urine showed the presence of a trace of albumin without casts, and there was a total absence of bile salts and pigments. W.B.C. count 10,600 per c.mm. No malaria parasite was seen. Although in the writer's experience blood culture was not found to be of any value on the 8th day of

illness yet it was done as Das Gupta and Chopra (1937) recorded a case which gave positive blood culture as late as the ninth day of illness. Two tubes of Vervoot's medium were inoculated with 0.1 and 0.2 c.cm. of blood respectively and 2 c.cm. of citrated blood was inoculated intraperitoneally into a young guinea-pig weighing 180 grammes approximately. The tubes failed to show any evidence of growth and the animal also remained well and alive during the observation period of 6 weeks. No leptospiræ could be detected in the peritoneal fluid of this animal. A part of the serum from the same sample of blood used for culture and animal inoculation was put up against a classical strain isolated locally and it reacted to a titre of 1 : 1,280. No further sample of blood or urine could be collected, as the patient left the hospital. The temperature came down to normal on the very day the patient was examined. However, the patient was later seen in his house and the case appeared to be a mild one. Thus the recovery was uneventful.

In this connection Walch-Sorgdrager (1939) pointed out in her monograph that of the cases observed in the Netherlands, those without jaundice had a more favourable issue than those with jaundice. Only one fatal anicteric case was reported, but even in this, the death was due to a complication.

With a view to shedding further light on the incidence of such forms of infection, samples of sera were examined for the presence of agglutinins against leptospira which were forwarded to this Institute for routine serological tests. These specimens were received from physicians and hospitals from all parts of the city. Only those sera were selected which gave a negative Widal reaction against the enteric group of organisms and in which the clot culture also proved negative. Each serum was put up against three classical strains, two of which were isolated locally, and, for each serum, dilutions ranging from 1 : 10 to 1 : 160 were employed against each antigen. Higher dilutions to detect the end titre were used where necessary. In all, 150 samples of sera were examined, of which only one showed a titre of 1 : 640. This sample of serum was not bile-tinted. The titre obtained is considered as indicating an active infection, and it has been shown that an antileptospiral titre of 1 : 100 is definitely suggestive of infection, since samples of sera from cases in which the disease could be excluded failed to react even in a dilution of 1 : 20 against the classical strains. Further tests were made on 75 samples of sera collected at random from the blood specimens submitted to this Institute for Wassermann reaction (Lahiri, 1942) and agglutinins could not be demonstrated in any except one which gave a doubtful reaction in a titre of 1 : 10 only.

Summary and conclusions

Two cases of leptospirosis without icterus are recorded, the diagnosis being based on serological tests. In one of the cases detected, the serum had been sent for a Widal test, leptospirosis apparently not having been suspected in the absence of jaundice.

Acknowledgment.

My grateful thanks are due to my colleague Dr. D. W. Soman, officer-in-charge of the diagnostic department for the supply of sera.

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THE OCCURRENCE OF LEPTOSPIROSIS IN ORISSA

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DAS GUPTA and CHOPRA (1937) discovered leptospirosis in India and reported first a bacteriologically positive case from Calcutta. Since then, several proven cases of infectious jaundice have been recorded from Calcutta, Assam and Bombay by various workers, *viz.* Das Gupta (1938, 1939, 1941), Konar *et al.* (1939) and Lahiri (1941, 1943). Though the discovery aroused considerable interest, the number of cases so far reported is small; but this is more due to lack of facilities for thorough laboratory investigation than to the rarity of cases.

The subject-matter of this report is a case of jaundice with fever, in which leptospiræ were found on examination of the centrifuged deposit of urine; the patient's serum however did not agglutinate the classical strain of *Leptospira icterohæmorrhagiae*.

Case report.—A Hindu male, aged 42, sub-inspector of police, was admitted on 2nd September, 1944, into the Police Hospital, Puri, for the treatment of hæmatemesis, melæna and jaundice.

History.—Twenty-six days before his admission into the hospital, he had a sudden onset of fever with general muscular pain, nausea, vomiting, photophobia, congested conjunctivæ and abdominal discomfort. The temperature was moderate and continued nearly for 4 days and then subsided with the appearance of jaundice, which gradually deepened. On 27th August, 1944, he had hæmatemesis for the first time, and from the next day he began to pass tarry stools daily. In a period of 2 days just preceding the date of admission, he had hæmatemesis 3 times.

On admission, temperature 97.6°F.; pulse 82 per minute; respiration 22 per minute; blood pressure 120/65 mm. Hg.; conjunctivæ intensely icteric; skin and mucous membrane yellowish; liver enlarged 2 fingers below the costal margin, tender, soft, smooth and movable with respiration; spleen not palpable; no abdominal rigidity, immobility or tenderness.

The patient had no ulceration on his penis, scrotum or any other part of the body.

Laboratory findings: *Stool.*—Tarry colour; benzidine test for presence of blood positive; on microscopical examination of several slides no protozoa or ova of helminths seen.

Blood.—No malaria parasite was found on repeated examinations of thick and thin blood films after prolonged search.

Total W.B.C.—10,800 per c.mm. of blood.

Differential count—

Polymorphonuclear	..	72%
Lymphocytes	..	23%
Monocytes	..	4%
Eosinophils	..	1%
Hæmoglobin	..	65%

Wassermann reaction—negative.

Qualitative van den Bergh reaction—direct biphasic strongly positive.

Agglutination reaction against *Leptospira icterohæmorrhagiae* (classical strain)—negative.

Urine.—The urine was collected with scrupulous care and under aseptic conditions. Total quantity in 24 hours—36 oz.; specific gravity—1017; high coloured, bile salt and pigment present; albumin, sugar, cells and casts not found.

On the advice of Dr. K. N. Misra, Civil Surgeon, midstream urine was collected and 100 c.cm. of this was centrifuged as advocated by Knowles (1928) and the centrifuged deposit was stained (Fontana) and examined daily for some days. Altogether 6 samples were examined in this way in 6 days. In 2 samples, spirochætes morphologically closely resembling leptospiræ were found in fair numbers. Morphological picture of some of the spirochætes was very clear.

Guinea-pig inoculation was not possible.

Hæmatemesis and melæna stopped with injections of vitamin K (Kaplin) and congo red. Gradually the patient recovered with daily intravenous injections of glucose and milk diet for 2 weeks. Jaundice disappeared, and he was discharged cured on 10th October, 1944.

Discussion.—The clinical picture of the case was not typical of leptospirosis, specially as regards urinary symptoms, but it is a well-known fact that the signs and symptoms of this disease vary very much. There occur cases so mild as to evade recognition altogether. Moreover, the existence of sub-clinical infection has been proved beyond doubt by Davidson and Smith (1939). They examined the blood of a group of healthy fish workers, 24.3 per cent of whom gave positive sero-reactions against leptospiræ.

In the present case, there was no toxic nephritis (at least when the patient came to the hospital), not even a trace of albumin in urine, and this is noteworthy. Such cases probably do occur. Rees (1939) and Sladden (1939) reported a case in which no urinary symptom was present and only a trace of albumin was present in urine examined on the 14th and 16th days of the disease. The case under report came very late in the 4th week of the disease. The slight febrile albuminuria that was present might have cleared up by the time he sought admission into the hospital.

A negative examination with a single strain does not exclude the possibility of leptospirosis as there are so many strains and serological groups. Das Gupta (1939) himself records a case, which did not show any agglutination

with the local strain (Chopra's strain, Calcutta) but reacted in a high dilution with a rat strain of Semurang (Java), giving some para-specific reaction with some other strains, including the classical strain of Wijnbergh. It is quite likely that had more complete serological examination been done, the serum of this case might have reacted with some strain.

Animal inoculation, immunological protective experiments and biochemical examinations were not done. The demonstration of leptospira on microscopical examination of centrifuged deposit of urine is not enough to put the diagnosis beyond doubt. The identification of leptospira was purely based on morphological characters, and it might be fallacious. The organisms found might be either true leptospira or some other non-pathogenic spirochæte morphologically closely resembling leptospira. The morphological picture was so clear that it seemed impossible that the appearance was produced by an artefact. I have not seen in the literature any mention of the presence of non-pathogenic spirochætes in the urinary tract of human beings, though several such organisms have been recovered from human faeces. Hence I am inclined to exclude non-pathogenic spirochæte and take the organisms as a true leptospira. The patient gave no history of syphilis and his Wassermann was negative. He had no phagedenic ulcer. Extraneous contamination of urine cannot be considered likely as we took so much precaution to avoid it. Taking all these facts into consideration the case seems to be one of leptospirosis.

Acknowledgment

I am very grateful to Rai Bahadur Dr. B. M. Das Gupta, Professor of Protozoology and Director, Calcutta School of Tropical Medicine, who kindly examined the blood serum and to Rai Saheb Dr. K. N. Misra, M.B., D.T.M., Civil Surgeon, Puri, for guidance and verifying my finding of leptospira in the centrifuged deposit of urine.

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[Dr. B. M. Das Gupta writes: 'In most cases of Weil's disease the albumin disappears from the urine in about two weeks. It is therefore not unusual to find no albumin on the 26th day. It is however very unusual in Weil's disease to have hemorrhages occurring as late as the 20th day. Non-pathogenic spirochætes have occasionally been reported in the urinary tract.'—Editor.]

THE UNSUITABILITY OF WHITE MICE FOR STUDIES OF LEPTOSPIROSIS

By M. N. LAHIRI

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LARSON (1941) recorded that young white mice (*Mus musculus*) are extremely susceptible to infection with *Leptospira icterohæmorrhagiae*, and when infected develop before death signs of generalized infection. Three-weeks-old mice were found to be most susceptible, and it was pointed out that there was a general decreasing mortality when older mice were used. The failure of previous workers to transmit the infection was possibly due to the lack of proper attention with regard to the age of the experimental mice. Encouraged by these observations, investigations were undertaken with a view to determining the suitability of young white mice for the laboratory studies of leptospirosis as there is an obvious advantage in the use of this animal over that of the guinea-pig, especially because of its cheapness. While the experiments were being planned, Das Gupta (1942) reported that young white mice are much less susceptible to the Indian strains of *Leptospira icterohæmorrhagiae* and are not suitable for carrying out the protection tests. It then seemed possible to attribute this to the particular breed of mice employed, as different ones vary in their susceptibility to yellow fever virus.

Materials and methods

Two strains of leptospiræ, one isolated from a patient and the other from a local rat, were used. The strains were perpetuated in Vervoot's medium and their virulence maintained by passage through young guinea-pigs approximately every four weeks.

Three-weeks-old Haffkine Institute inbred mice were used for each strain. Intraperitoneal inoculations were made with varying doses of each culture ranging from 0.2 to 0.6 c.cm. For each dose 3 mice were employed along with a young guinea-pig weighing about 150 grammes to serve as a control, which received 1 c.cm. of the test dose of the cultures. The animals were kept under observation for a period of 3 weeks. Out of the 36 mice used in these experiments, only one showed evidence of infection on the seventh day of inoculation with a test dose, 0.5 c.cm. of the culture of the human strain. There were definite signs of jaundice, most marked in the ears, in this animal before death. The organisms were recovered in pure culture from the heart's blood. The control guinea-pigs at each instance died of the infection exhibiting typical post-mortem signs, and their liver suspensions showed leptospiræ in considerable numbers. Thus, the Haffkine Institute inbred mice were found to be fairly resistant to the local strains of leptospira.

A good herd of the Javanese mice was raised. Three-weeks-old mice in batches of three were

used for each dose of the culture. In these experiments, however, the dosage of the cultures varied from 0.2 to 0.5 c.cm. inoculated intraperitoneally in the same manner. In all, 30 mice were used of which two died of leptospiral infection, one having received 0.5 c.cm. of the culture of the human strain and the other 0.3 c.cm. of the rat strain. The control guinea-pigs all succumbed to the infection following inoculation with 1 c.cm. of the test dose of the cultures. These experimental results demonstrate that Javanese mice are also fairly refractory to infection with the strains of leptospira used.

Larson (*loc. cit.*) pointed out that 0.6 c.cm. of an infective material could also be injected into young mice conveniently by the intraperitoneal route. A litter of 6 mice, exactly three weeks old, was selected from a stock of the Swiss strain of mice maintained in this Institute. They were similarly inoculated, the infective agent being a suspension of the liver of a guinea-pig used for passing the rat strain. The suspension showed leptospiræ in large numbers. In the series all survived.

Summary

Three-weeks-old Haffkine Institute inbred mice and Javanese mice were inoculated with varying doses of two virulent cultures of *Leptospira icterohæmorrhagiae* in batches of three. In the first series all survived but one, while in the second series of the 'Javanese' mice there were only two deaths due to infection. The control guinea-pigs all died of infection between the fifth and seventh day. In a third series of six 'Swiss' mice also all survived. These experiments, therefore, lend support to Das Gupta's findings and clearly indicate that young white mice are not suitable for the laboratory studies of leptospirosis in this country.

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SULPHAPYRIDINE IN GONORRHOEA

By P. V. KARAMCHANDANI, M.B., B.S., F.R.C.P.

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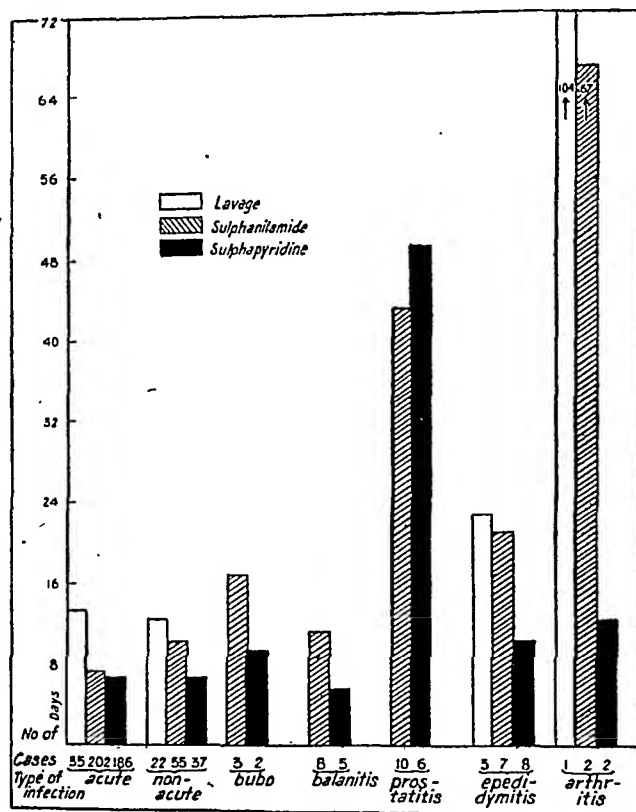
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PENICILLIN has now come to the forefront in the treatment of gonorrhœa, but it is not generally available. In this connection it is worth remembering the comparative value of older forms of treatment. This paper presents an analysis of 594 cases of gonorrhœal infection treated by the authors under conditions of close observation. Sixty-one cases were treated with permanganate lavage, 287 with sulphanilamide (four grammes per day for 5 days) and 246 with

sulphapyridine (six grammes first day, five grammes second day, four grammes third day and fourth day). Cases of uncomplicated gonorrhœa are divided into two stages: (i) Acute—The patient usually arrived with purulent discharge and acute symptoms, *viz.* burning, smarting during micturition, redness of the meatus, œdema of the penis, etc. At this stage the smear usually showed many pus cells, gonococci and few epithelial cells. (ii) Non-acute—With mucopurulent, mucoid or watery discharge, where the intensity of inflammation was less, pus cells and gonococci being fewer, while epithelial cells were in greater numbers; or alternatively pus cells comparatively more (five or ten to one of epithelial cells) and fewer gonococci (mostly extracellular).



It will be seen from the graph that the average period of cure with sulphapyridine in cases of gonorrhœa is under 7 days in uncomplicated cases, and in those complicated with balanitis, while it was under 10, 11, 13 and 50 days in those complicated with bubo, prostatitis, metastasis (in joints) and epididymitis, respectively.

These results, when compared with those obtained with sulphanilamide, show a distinct improvement except in acute gonorrhœa and prostatitis, where the results are almost equal. The number of cases with various complications is too small, but that under uncomplicated gonorrhœa is large enough to justify statistical evaluation.

Other advantages that were noticed with sulphapyridine treatment were that it required fewer repetition courses in the cases that did

not respond, there was very little need for use of vaccines, etc., and the relapse rate was extremely low. The vaccine given was the mixed gonococcal vaccine from Kasauli administered in three graduated doses bi-weekly. When milk was combined with it, the first dose of 3 c.cm. was given intramuscularly, and increased by one c.cm. bi-weekly till 8 c.cm. were reached. Milk was given when the full course of vaccine had not proved effective, and it helped to effect cure.

It will be seen that when penicillin is not available, sulphapyridine is the drug of choice.

BRONCHIAL ASTHMA AND PULMONARY TUBERCULOSIS

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THERE is a common belief that bronchial asthma and pulmonary tuberculosis do not

tuberculosis, and (c) bronchial asthma and non-pulmonary tuberculosis.

Bronchial asthma and pulmonary tuberculosis

In this series there were 91 cases of asthma and among them 15 patients (16.5 per cent) developed tuberculosis. Of these 15 cases, 13 had x-ray examinations which showed unilateral disease in 6, and bilateral in 7. The lesions were mostly exudative; one had breakdown and another definite cavities. The sputum was positive in 9 cases, negative in 5, and not examined in the last. The asthmatic symptoms were wheezing with râles and rhonchi scattered over both lungs with prolonged expiration; eosinophilia above 4 per cent in 8 and above 20 per cent in 3. In 11 cases tuberculosis appeared 2 to 15 years after the onset of asthma. The details of the 15 patients are given in table I.

Two other patients who had râles and rhonchi in both lungs and blood eosinophilia of 57 and 10 per cent respectively had never any dyspnoea.

TABLE I
Asthma cases with pulmonary tuberculosis

Case number	Age	Sex	Age at onset of		Eosinophil, per cent	Sputum	X-ray lesion in lungs	REMARKS
			Asthma	Pulmonary tuberculosis				
1	31	F.	25	31	5	Negative	Both	Worse.
2	36	M.	24	36	2	Positive	Right lung	Worse. Thirteen artificial pneumothorax then discontinued.
3	31	M.	23	31	4	Do.	Left lung	Stationary. Ten artificial pneumothorax. Now on gold.
4	32	M.	20	32	2	Do.	Do.	Died in 6 months.
5	40	M.	33	40	8	Not done	Do.	Died.
6	28	M.	26	28	54	Negative	Both	Cured with rest, soamine and gold, 1 year.
7	40	F.	38	40	1	Positive	Do.	Worse.
8	70	M.	55	70	6	Negative	Left lung	Stationary.
9	28	M.	Not known		32	Positive	Both	Worse.
10	24	M.	Do.		80	Negative	Do.	Cured.
11	46	F.	Do.		9	Do.	Left lung	Better.
12	22	M.	14	22	8	Positive	Not done	Lost trace.
13	45	M.	40	45	8	Do.	Do.	Do.
14	50	M.	Not known		6	Do.	Both	Stationary.
15	39	M.	32	39	6	Do.	Do.	Do.

occur together; yet in the writer's experiences the combination is sufficiently common to warrant examination of any case of bronchial asthma for evidence of tuberculosis in the lungs. The object of this paper is to study the relationship between the two diseases in a series of 572 cases seen during the years 1943 and 1944 at this hospital, of which 481 had pulmonary tuberculosis, 76 asthma, and 15 had both. Those with asthma and pulmonary tuberculosis are divided into the following three groups: (a) bronchial asthma and pulmonary tuberculosis, (b) bronchial asthma as a sequel to pulmonary

Bronchial asthma as a sequel to pulmonary tuberculosis

There were only two such cases.

One patient, a clerk, 26 years, had hæmoptysis in December 1939 and was x-rayed after a month. He had artificial pneumothorax treatment for 7 months and a phrenic operation thereafter. He was then given gold injections, after the third of which he developed typical bronchial asthma for the first time, and suffered from it for 3½ years. Later x-rays showed no evidence of tuberculosis of the lungs. He was given soamine (24), autohæmotherapy (6), autovaccine (2 courses) and later tuberculin (B.E.) up to 1/100 mg. apparently with no immediate benefit.

The second patient, a doctor, 36 years old, had bilateral disease. Artificial pneumothorax was performed for 4 months, then a phrenic operation was done. He was also given gold injections. Thereafter, he developed typical asthmatic symptoms, and is still suffering from it. Wheezing seems to have become permanent with exacerbations at times; anti-spasmodics and soamine had no effect, but tuberculin (B.E.) seemed to have diminished the intensity of his symptoms.

Bronchial asthma and non-pulmonary tuberculosis

One asthmatic patient had tuberculous glands in the neck without similar affection of the lungs. Another had tuberculous osteomyelitis of the rib. The details of these cases are given below.

of 167,000 cases by mass radiography and represents the largest series so far studied.

Among the 496 (481 + 15) cases of lung tuberculosis, 15 (3 per cent) had bronchial asthma at some period or other. Tocker and Davidson (1944) reporting on 386 cases of active pulmonary tuberculosis from Sea View Hospital found that 12 cases or (3.1 per cent) presented a history of bronchial asthma. This figure approximates to the incidence of asthma among the normal population. Thus, Rowe (1937) reported 3 per cent asthma among 1,600 University students examined in California, and Service (1939) 3.67 per cent among 3,141 individuals in the city of Colorado Springs. It

TABLE II

Age	Sex	Family history	Eosinophil, per cent	Type of lesion	REMARKS
28	F.	T.B. lungs	15	T.B. cervical gland	X-ray negative. Asthma 2 years before gland involvement.
30	M.	Asthma	Not done	T.B. osteomyelitis 6th left rib.	Fluoroscopy negative. Asthma 10 years before osteomyelitis.

Prognosis in patients suffering from both bronchial asthma and pulmonary tuberculosis

The course and prognosis in these cases appear to be worse than those of pulmonary tuberculosis uncomplicated by asthma. In the present series, two cases were cured, one is better, four more or less stationary, four have become worse, two died, and two could not be traced.

Treatment of patients suffering from both bronchial asthma and pulmonary tuberculosis

Treatment is the same as that of pulmonary tuberculosis. Mild cases respond to rest, gold and soamine. Others may require artificial pneumothorax which is not contra-indicated in asthma cases complicated with pulmonary tuberculosis, except during the acute asthmatic fits. In this series it was performed in 3 cases and caused no breathing difficulty; it was however discontinued by the patients after 13, 10 and 8 sittings. A fourth case (not included in the series) who also had this treatment was interesting. He was a Hindu male, aged about 48 years, and had diabetes, asthma and bilateral tuberculosis. He was given simultaneous bilateral pneumothorax, 22 being given in the course of six months. He did not experience dyspnoea in spite of bilateral treatment, a past history of asthma and a fairly advanced age. Subsequently he left Calcutta and was lost sight of.

Discussion

The incidence of pulmonary tuberculosis in the normal population is less than 1 per cent (0.82 per cent Brooks, 1943). Other studies put it at a slightly higher level. But Brooks' figure is given, as it is based on a study

may thus be assumed that tuberculosis of the lungs does not predispose to bronchial asthma.

In the present series of 91 cases of asthma 15 (16.5 per cent) were found to suffer from lung tuberculosis. Fraenkel (1934), in a similar study, found its incidence in 16.7 per cent among 369 asthma cases and Harkavy and Hebal (1930) reporting on 400 asthmatic cases from Mount Sinai Hospital found that 10 per cent were tuberculous.

The incidence of tuberculosis among asthmatics is therefore 12 to 20 times higher than in normal population. There are two factors which may be partially responsible for the high incidence of tuberculosis among asthmatics in the present series. More asthma cases are probably seen in the general medical out-patients' than in a chest clinic, where only those with suspected tuberculosis are usually seen. Further, if statistics were collected over a longer period, say a ten-year period, this incidence might have been less high.

There has been a view in the past led by Landouzy that all or the majority of cases of asthma were of tuberculous origin. The tubercle bacilli are widely scattered, and the incidence of tuberculous infection among the town-dwellers is very high. The hypersensitiveness in asthma may thus be acquired in the first instance from contact with the tubercle bacilli. But against this view it may be pointed out that all asthmatics do not react to the tuberculin skin test (Pirquet, Mantoux or Patch test), and therapeutically too, all asthmatics do not respond to tuberculin. Incidentally, it may be pointed out that Maxwell's results with tuberculin in asthma cases were much less promising in 1932 than in his earlier reports in 1930.

Does tuberculosis benefit asthma or *vice versa*? Some observers have reported that active tuberculosis benefits asthmatics. During the phase of active tuberculosis, asthmatic fits either do not occur at all or are much lessened in frequency—but when the tuberculous disease heals, asthmatic fits recur. Such beneficial effects were not observed in the present series.

It has been argued by other observers that asthma favourably influences the course of tuberculous disease, and that the fibroid form is more common among asthmatics. The findings in the present series are contrary to this view; the lesions were predominantly exudative in type—one had breakdown, and another had definite cavities. In Harkavy and Hebdal's (1930) series 17 out of 40 cases or 42.5 per cent showed cavities. Fraenkel's (1934) cases however showed more fibrotic changes; among his 62 cases, 16 had active tuberculosis, 26 productive inactive cirrhotic lesions and 20 had healed lesions.

Moreover, it may be pointed out that asthma cases may exert a harmful effect on tuberculosis. The excessive cough and increased secretion may help the bronchogenic spread in an active case. Also the tendency to re-expansion of the lung and consequent re-opening of cavities observed in asthma cases undergoing artificial pneumothorax treatment by Vaccarezza and Cucchiani (1941) interfere with effective collapse therapy.

Summary

Statistics show that the incidence of asthma in the tuberculous group and in the normal group is almost the same. But the incidence of pulmonary tuberculosis among asthmatics is 10 to 20 times higher than among normal individuals. Among 91 cases of bronchial asthma 15 had pulmonary tuberculosis.

Two cases of arrested lung tuberculosis in this series developed bronchial asthma as a sequel.

Bronchial asthma appears to predispose to pulmonary tuberculosis. Further, the fits of cough and increased secretion may help the bronchogenic spread in an active case of tuberculosis; and the condition of asthma interferes with effective collapse therapy.

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[Three out of the 15 cases of asthma plus pulmonary tuberculosis are recorded as showing an eosinophil count of 32, 54 and 88 per cent. One cannot help wondering whether these were really cases of tuberculosis and asthma. Is it not possible that they were

cases of the so-called 'tropical eosinophilia' in which the clinical and x-ray findings sometimes lead to a wrong diagnosis of tuberculosis? This suggestion is supported by the fact that two out of these three cases are recorded as cured with rest and injections of arsphenamine and gold. Moreover, these are the only two out of the 15 cases in which cure is reported.—EDITOR, I.M.G.]

AN EASY METHOD OF PRODUCING PERMANENT ROUGH VARIATION IN CHOLERA VIBRIOS*

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ROUGH cholera vibrios are required to prepare rough sera, and rough sera are used to test smoothness of cholera vibrios and also the potency of cholera vaccines. Hitherto only one rough strain of the Inaba sub-type was available at the Central Research Institute, Kasauli, but none of the rough Ogawa sub-type. Cholera vaccines were therefore being tested with Inaba rough serum and not with Ogawa rough serum, although the vaccine is nowadays made up of both Inaba and Ogawa sub-types of the smooth vibrios. A method of producing a rough variation in the cholera vibrio is as follows:—

A nutrient agar plate with 1 in 5,000 atebrein (Bayer) incorporated in the medium is prepared, and on it Inaba and Ogawa smooth vibrios are streaked. The vibrios begin to grow on such a medium, and after a few days, rough colonies appear here and there in the streaked area. These are re-plated on ordinary nutrient agar medium. If no rough discrete colonies are seen, re-plating is done on atebrein-agar medium so as to isolate the rough colonies.

An Inaba rough colony is 1 to 2 mm. in diameter in 48 hours, glistening, slightly opaque with a crenated margin. The growth on agar slope is fine and scanty. Microscopically, some organisms show typical comma forms but some show either straight, spherical or ovoid forms. The organism is sometimes non-motile. It sometimes ferments lactose, producing acid only. In glucose, saccharose, mannitol and maltose, acid only is produced. The cholera-red reaction is positive. The organism is salt-sensitive and gives a positive Milton's test. With Inaba rough serum it is agglutinated to full titre but with Inaba smooth serum it is agglutinated only partially. For example, the Inaba smooth is agglutinated up to 1 in 400 with Inaba rough serum, whereas the induced Inaba rough is agglutinated up to 1 in 1,600. *Vice versa*, with Inaba smooth serum, the original strain is agglutinated to full titre but the rough strain to a very low titre. This variation is maintained

* The paper was read before the Indian Science Congress Association, held at Nagpur in January 1945.

and there is no reversion to the smooth form. All strains cannot be readily converted into rough forms by this procedure.

An Ogawa rough form grows scantily in fine colonies which are sometimes non-glistening, opaque and flat with crenated margins and rough surface. Microscopically, comma forms as well as long straight forms are seen. The organism is motile, ferments lactose initially, but later acidity is followed by neutrality. Glucose, saccharose, mannitol and maltose are fermented with the production of acid only. The cholera-red reaction is positive. The organism is salt-sensitive and gives positive Milton's test. With Ogawa smooth serum, the original strain is agglutinated up to 1 in 4,000, but the induced rough strain is agglutinated up to 1 in 50 only. The variation appears to be permanent.

TURMERIC AND VEGETABLE OILS AS REPELLENTS AGAINST ANOPHELINE MOSQUITOES

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In the course of a malaria survey of elementary schools, Major R. Senior White investigated the splenic index in boys and girls in two localities. One was Koraput, situated in the hyperendemic Jeypore hill tracts in Orissa, but the children belonged mostly to the police staff hailing from Ganjam and North Vizagapatam districts. The other locality was Naupada, a village in the North Vizagapatam coastal area; in this locality observations were made both before and after malaria control measures were adopted. The figures are reproduced below.

in boys; and that at Naupada, following malaria control measures, the splenic index in both sexes was halved but the male-female ratio in splenic index remained unchanged.

Somewhat similar results were obtained by Russell *et al.* (1938) in South Madras, which are given below.

TABLE II

Sex	Number examined	Number palpable	Spleen index
Males ..	3,292	1,308	39.7
Females ..	1,358	411	30.3

It appears therefore that the male sex in these localities is more exposed to infection than the female sex.

In the course of investigations on the feeding and resting habits of the fluviatilis group of anopheline mosquitoes in the Jeypore Hills, involving adult mosquito catches as they enter and feed in houses at night, a curious fact was observed. Every one of the mosquitoes was found to feed on men only, though women were also sleeping close at hand. These catches were made in houses occupied by the subordinate railway staff belong to the local Khond and Oriya tribes (it would be difficult to attempt such catches in the houses of the Telugu staff hailing from the plains of the North Madras coast). Sex *per se* cannot of course explain this phenomenon, but it may be due to some peculiarity in the personal habits of these women. On enquiry it was found that these women take their daily bath after application of turmeric and mustard or gingili oil to their bodies and do not use soap during the bath. This custom is a *sine qua non* of the married state and maidenhood, but widows are prohibited its use.

TABLE I

Date	Locality	SPLENIC ENLARGEMENT														
		Boys								Girls						
		No. exd.	Nil	1 fb.	2 fb.	3 fb.	4 fb.	5 fb.	Spleen index	No. exd.	Nil	1 fb.	2 fb.	3 fb.	4 fb.	Spleen index
Jan. '37	Elementary Schools, Koraput.	114	66	10	16	8	10	4	42.1	53	41	3	4	4	1	22.7
20-3-43	Elementary Schools, Naupada.	80	52	20	3	3	2	..	35.0	30	28	2	6.7
10-3-44	Do.	83	69	6	4	1	3	..	16.9	51	49	2	3.9

fb. = finger breadth.

It will be observed that in both areas the splenic index was much lower in girls than

The use of turmeric and gingili oil was probably universal at one time, but now among

the economically better off and socially more advanced women, soap is used and the use of turmeric and mustard or gingili oil is confined to certain ceremonial occasions.

To ascertain whether turmeric and vegetable oils have any repellent effect, the following tests were made: The first author collected in the Jeypore Hills over a dozen anopheline mosquitoes, mostly *A. fluviatilis*, in a cage and put inside it one of his hands previously besmeared with turmeric and mustard oil and then washed with plain water. The mosquitoes refused to feed on it whereas immediately afterwards they rapidly fed on his other hand not so besmeared. He repeated the experiment next night with the same result. About the same time, the second author carried out a similar experiment using gingili oil instead of mustard oil with *A. subpictus* and *A. annularis* at Naupada (North Madras Coast) with precisely similar results.

Since the above observations were made, we came across, by the courtesy of Major R. Senior White, the statement made by Bispham (1944) which bears on our findings. He says that, in certain tropical countries, local habits of the population either limit the spread of malaria or increase the spread. In Fezzan, for instance, women are not often infected because they anoint their bodies, as a cosmetic habit, with an oil which is deterrent to mosquitoes. On the other hand, small children in most hot countries wear no clothing until they are six or even more years of age and are easily bitten by the infected mosquito.

Summary

(a) Turmeric and vegetable oils appear to exercise a repellent effect against anopheline mosquitoes.

(b) The relative freedom from malaria of women in the Jeypore Hills and in the bilingual areas of the North Madras Coast may be attributable to their habit of besmearing themselves with these two substances before their daily bath.

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TROPICAL ULCER

A STUDY OF ONE HUNDRED CASES COLLECTED IN THE CITY OF MADRAS

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At the Stanley Hospital, Madras, a study of tropical ulcers (*Ulcus tropicum*) was first started on 27th November, 1943, at the request of the superintendent. A few cases were investigated, but subsequently they became scarce at the hospital. Later it was observed

that a large number of cases of tropical ulcer were attending the dispensary conducted by the Ramakrishna Mission at Mylapore. With the kind assistance of the authorities of the Mission and the medical officer of the dispensary, the ulcers were investigated. A total of one hundred cases formed the series under investigation.

The ulcers were recognized as 'ulcus tropicum' by their indolent nature, shelving base, often foul-smelling profuse discharge, and the associated pain and tenderness. The diagnosis was confirmed by the presence of Vincent's bacillus either alone, or with spirochaetes in the discharge.

The following observations were made:—

The size of ulcers varied from $\frac{1}{4}$ inch to $2\frac{1}{2}$ inches. Of 84 ulcers, 73 did not exceed one inch in diameter. Most of the ulcers were circular or oval. Of 95 ulcers, 62 were on the foot, 32 on the leg, and one on the elbow.

Pain was almost invariably present which rendered the patient often sleepless. The ulcers were very tender. Twelve out of 84 cases examined showed enlarged lymph glands. In these, there was associated inflammation of the cellular tissue surrounding the ulcer.

Age incidence

Below 7 years	7-15 years	15-30 years	30-50 years	Above 50 years	Total examined
Nil	28	39	14	9	90

The lowest age at which the ulcer was noted was in a boy of seven years. The largest number occurred among adults engaged in active work.

Sex.—In a total of 98 patients in whom the sex was recorded, there were 88 males and 10 females.

Occupation and history of injury (see table).

In the group 'others' are included 19 school children in addition to persons following occupations such as toddy tapping, goldsmith, barber, etc.

Comment.—The highest number was among the weavers. Only 4 out of the 30 weavers gave a history of injury as a provocative cause for the ulcer. This is interesting, since, nearly 50 per cent of other cases have given a history of injury. The weavers also admitted that these ulcers were very commonly prevalent among them.

Treatment.—No controlled experiments were conducted. The impression formed is that mere antiseptic treatment such as the application of gauze soaked in 1 in 40 lysol lotion or eusol lotion was not effective. Ointments such as boric acid and zinc oxide were equally useless. The discharge freely oozed out of the ulcer through the dressings, the margin gradually extending under the discharge.

Gauze soaked in warm 5 per cent copper sulphate solution was found to be very effective, reducing the discharge in about 3 to 7 days. Thereafter healing took place rapidly.

forms of Vincent's bacilli were non-motile while the long forms were more slender, and motile. In addition to the spirochaetes and Vincent's bacilli, *B. proteus* and some other very actively

	Weavers	Coolie	Domestic servant	Cart driver	Carpenter	Others	Total examined
Total in each group ..	30	7	7	2	2	43	91
With history of injury ..	4	3	4	2	2	20	35
Without history of injury ..	26	4	3	0	0	23	56

Epidemiology

The possible factors that lead to the incidence of 'ulcus tropicum' appear to be :—

1. *Trauma*.—If the weaver group is excluded from the series, it will be apparent that nearly 50 per cent (31 out of 61) give a history of injury initiating the sore.

2. *Bites by insects*.—A high proportion of the ulcers were among the weavers (30 out of 91). In this 30, only 4 gave a history of injury initiating the ulcer, while 26 did not. Another feature observed is that among the weaver group, with the exception of 2, all were adults above 15 years. All these people were males. These men evidently had been engaged in their vocation of weaving in their houses. The occupation necessitates them keeping their legs in pits for long hours. These pits are long pits in which the handlooms are lodged. The pits are kept moist, warm and lined with cowdung. Insect larvæ and adult insects may be sheltered in the pits. Whether insects have anything to do with initiating the ulcer has to be investigated.

3. *Nutrition*.—It was a common observation made during the study of this series that the class of patients coming with these ulcers consume little or no milk.

Bacteriological observations

Microscopic examination was done at first by staining the smears from ulcers by Gram's stain, but later on freshly diluted carbol fuchsin stain was substituted.

Total specimens examined	Fusiform bacilli alone present	Fusiform bacilli and spirochaetes present	Long forms of fusiform bacilli present
100	48	44	14

Streptococci and staphylococci alone were found in 8 cases which did not resemble the typical tropical ulcer in all respects. The short forms of Vincent's bacilli were tapering at the ends and slightly curved. They were seen in large numbers.

Examination of wet preparations by dark ground illumination showed that the short

motile bacilli (*Ps. pyocyanea*?) and some cocci were seen.

The long forms of Vincent's bacilli were fewer in number and were seen at a deeper level. Any current in the preparation could not disturb these organisms very much. The motility was very characteristic, namely, a lateral oscillatory movement of the progressing end, and a bending and straightening of the whole length of the organism. The bacilli could often be seen progressing slowly across the field. Fox (1921) has described motile Vincent's bacilli in wet preparations. He describes them as 'having a peculiar wriggling movement suggestive of mosquito larvæ.' Smith (1933) describes motile fusiform bacilli in wet smear preparations from tropical ulcer cases.

Cultural examinations.—The medium used was that of Smith (1930) described as modified Wenyon's medium. Instead of human blood, rabbit blood was used. The fusiform bacilli grew along with *B. proteus* and other organisms. It took about three days to one week for the fusiform bacilli to multiply. The spirochaetes were alive for the first few days, but failed to multiply.

Total cultures examined	Fusiform bacilli grown
39	12

In seven cases in which the long forms of fusiform bacilli were seen from the direct smear, positive cultures were obtained. The organisms showed the same kind of motility. They were slender, adhering to masses of cellular debris especially decaying leucocytes. Sheaves of the bacilli could sometimes be seen twisted round one another. Often they were seen arranged in a radiating manner around a central mass of cellular debris. In one case, however, these long forms showed no motility, and had a granular appearance. The appearance was identical both in direct smear as well as in culture.

Pure cultures of the fusiform bacilli were obtained in a few instances on solid media (one

per cent agar containing 25 per cent rabbit blood) incubated at 37°C. in an atmosphere of 90 per cent hydrogen and 10 per cent carbon dioxide. Sub-cultures could not be maintained; further attempts are being made.

Summary

A study of a hundred cases of 'ulcus tropicum' collected in the city of Madras exhibited the following features:—

1. The fusiform bacillus was present in every case of 'ulcus tropicum.'
2. A motile form of Vincent's bacillus is present in some of these ulcers.
3. The lower limbs form the site of election for the ulcers in almost all cases.
4. Though injury is responsible for starting the ulcers, there might yet be another factor in their causation, viz, the insect factor.

My thanks are due to Dr. C. G. Pandit, O.B.E., M.B., B.S., Ph.D., D.P.H., D.T.M., Director, King Institute, Guindy, for valuable suggestions and help in carrying out the investigation and for permission to publish these notes.

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APPLICATION OF THE D.E.C. MEDIUM TO THE ISOLATION OF TYPHOID BACILLI FROM SEWAGE IN CALCUTTA*

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As the D.E.C. medium of Panja and Ghosh (1943) is markedly inhibitory to coliform organisms, it was thought desirable to try it for isolation of *Bact. typhosum* from the sewage of Calcutta. This work was first undertaken here by Stewart and Ghoshal (1932) using the Wilson and Blair medium, and *Bact. typhosum* was isolated from the sewage. There are however certain disadvantages with the latter medium: it is more difficult to prepare; it has to be used on the same day that it is prepared; at least two or three plates have to be used for one sample of sewage; the suspected colonies are to be examined after 48 hours of incubation instead of 24 hours; recognition of the colonies is difficult; and the medium is often too soft for satisfactory work. We therefore wished to see whether our medium would remove the above disadvantages, and whether a higher percentage of isolation would be obtained.

The Wilson and Blair medium was prepared according to the latest formula given by Wilson and Blair (1931). First of all, it was tested with pure cultures of typhoid bacilli. After 24 hours' incubation, most of the colonies were greenish in colour, but a few were small and black with a metallic sheen. There was no further change after 48 to 72 hours' incubation. It may be mentioned here that on the D.E.C. medium, the colonies were about 2 mm. in diameter, smooth, slightly opaque and undifferentiated.

A loopful of young broth culture of the typhoid bacillus was mixed with about 12 c.cm. of sewage and plated direct on the Wilson and Blair medium. Eleven suspected black colonies were tested but none of them was of the typhoid bacillus. The mixture was plated again after 24 hours, and out of 14 colonies tested, 4 proved to be of typhoid bacilli. Similarly plating was done on the D.E.C. medium direct after mixing and again after 24 hours. In the first instance, 10 colonies were tested and all were of typhoid bacilli and in the second instance 3 colonies out of 4 tested were of typhoid bacilli. This simple preliminary experiment suggested the possibility that the new medium might be superior to the Wilson and Blair medium in the isolation of typhoid bacilli from sewage.

One hundred samples of sewage were collected from different pits in northern Calcutta and kept in the ice-chest for 15 to 30 minutes before plating. By practice, it was found that the sewage had to be diluted 1 in 3 before plating; otherwise colonies were so numerous that the isolation of typhoid bacilli was not possible. Large plates 6 inches in diameter were selected, one containing D.E.C. medium and two containing Wilson and Blair medium, for each sample of sewage. Plates were marked into 4 quadrants, and 4 drops of diluted sewage were put in one quadrant of the D.E.C. medium and 6 drops in the Wilson and Blair medium. Thus the total number of drops on two plates of Wilson and Blair medium was 12, i.e. three times more chance of success was given to this medium. Suspected colonies were fished out and streaked on small areas on MacConkey's plates. It was easier to select lactose-nonfermenting clear colonies from D.E.C. plates. This preliminary sub-culture on MacConkey's medium eliminated many colonies as lactose-fermenters and thus a lot of extra work was saved. The result of selection of colonies from the two media is given in the following table:—

	D.E.C. medium	Wilson and Blair medium
Total number of colonies fished out.	1,012	2,229
Lactose non-fermenters ..	858	1,146
Percentage ..	85	51
Identified as <i>Bact. typhosum</i>	7	1

*The paper was read before the Indian Science Congress Association held at Nagpur in January 1945.

The above result clearly shows how more mistakes are apt to occur in the selection of colonies from plate cultures on Wilson and Blair medium than from the D.E.C. medium. If two plates of the D.E.C. medium and 12 drops of sewage had been used, the number of successful isolations would presumably have been higher. It may be mentioned here that for identification of typhoid bacilli, slide-agglutination from colonies of primary cultures or sub-cultures on MacConkey's medium could not be relied upon. Sugar reactions and agglutination in Dreyer's tubes were done and where sugar reactions were suggestive but agglutination negative, Vi typhosum antiserum was used for agglutination.

It may also be mentioned here that vibrio colonies on D.E.C. plates are characteristically transparent, large, 2 to 4 mm. in diameter and low convex. Such colonies were not found in any samples of the sewage plated. No search for paratyphoid bacilli was undertaken.

Artificial mixtures of sewage and typhoid bacilli were treated with brilliant green (1 in 10,000) before plating, but such an enrichment method was found less successful. For example in one sample of sewage, out of 18 colonies of lactose-nonfermenters selected, 7 proved to be those of typhoid bacilli, whereas by the brilliant green method, only one colony of typhoid bacilli was found.

Summary

One hundred samples of sewage collected from different pits of Calcutta were examined by two methods—culturing on two plates of the routine Wilson and Blair medium and on one plate only of the D.E.C. medium of Panja and Ghosh for the isolation of typhoid bacilli. By the former method, although two plates were used for each sample, typhoid bacilli were isolated from one sample only, whereas by the latter method, using one plate only, typhoid bacilli could be more easily isolated from seven samples of the sewage. There are additional advantages of the D.E.C. medium over the Wilson and Blair medium. The D.E.C. medium is easier to prepare, can be used 3 or 4 days after preparation, can be kept sealed in paraffin-plugged Jena glass tubes for weeks for future use, and the medium being harder than Wilson and Blair medium, can be more easily inoculated. Only 24 hours' incubation is necessary after plating with a smaller inoculum, and suspected colonies on the plates are easier to recognize. On Wilson and Blair medium, there is more chance of missing the colonies of typhoid bacilli, as some colonies are black and some are green. Hence, only 51 per cent of the colonies selected from Wilson and Blair plates proved to be lactose-nonfermenters, whereas 85 per cent of the colonies selected from the D.E.C. medium were lactose-nonfermenters.

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RAPID METHOD OF PARAFFIN EMBEDDING

By P. V. GHARPURE

MAJOR, I.A.M.C.

As a result of several years' experience, I have found that acetone alone can be used quite efficiently and economically as a combined fixative, dehydrant and clearing agent in paraffin embedding. Pieces of tissue, roughly 1 cm. by 0.25 cm., can be passed through three successive baths containing about 10 c.cm. of acetone and then directly embedded in paraffin. The acetone in the first bath will be useless as a fixative any further, but it can with advantage be stored for washing capillary pipettes. The acetone in the second and third baths can be used as the first and second baths for fixing the next piece of tissue. Thus the cost for a section is negligible.

Where freezing equipment, viz, a special microtome and carbon dioxide, is not available, and when the ethyl chloride method is not possible, I have recently modified the technique as follows: The tissue is received in a test tube containing a mixture of commercial formalin 5 c.cm. and spirit 20 c.cm. and brought to boiling point in a water bath. It is then put on a filter paper and rolled to remove the excess of fluid and transferred serially into three acetone baths, keeping it for one hour in each. The tissue is next put in two melted paraffin baths also one hour in each. The block is cut immediately it is set. The whole procedure including cutting sections and staining can be completed in six hours.

EFFECT OF HEAT AND LIGHT ON THE ASCARIDOL CONTENT IN OIL OF CHENOPODIUM

By A. K. MUKERJI, M.B.

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 and

K. K. SEN GUPTA, M.Sc.
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In a previous paper (Mukerji and Ghosh, 1943), it was shown that there was a progressive deterioration of the ascaridol content in oil of chenopodium when it was kept at room

temperature varying from 70°F. to 98°F. whether protected from light or not.

To find out the best way of storing the oil with a minimum loss of the ascaridol content, the following experiments were conducted:—

Six samples of the oil were placed in glass-stoppered phials and kept under the following conditions for one year.

Sample A was exposed to direct sunlight for about five hours a day throughout the greater part of the year.

Sample B was kept in subdued light in a cool room where the temperature varied between 65°F. and 75°F. during the year.

Sample C was kept in the same room as above, but the bottle was covered with black paper.

Sample D was kept in strong diffuse light on the working table of the laboratory where the temperature ranged between 70°F. and 98°F. during the year.

Sample E was covered with black paper and kept inside a cupboard in the laboratory.

Sample F was kept inside the same cupboard but not covered with black paper.

Sample G was kept in the dark in an electric incubator at a constant temperature of 37°C.

At the end of two, four, six and twelve months the ascaridol content of the oil in these bottles was determined by one of us (K. K. S. G.) according to the standard B.P. method. The findings are shown in the following table:—

Sample	ASCARIDOL CONTENT, PER CENT					Total loss, per cent
	Initial	After 2 months	After 4 months	After 6 months	After 12 months	
A	68.6	62.5	60.3	57.9	56.0	18.4
B	64.7	63.8	63.2	62.8	61.4	5.1
C	64.8	64.1	63.5	62.9	61.6	4.94
D	65.2	63.1	61.05	59.8	58.2	10.7
E	66.0	64.5	63.8	63.4	62.2	5.76
F	66.4	65.8	64.6	63.9	62.6	5.76
G	66.9	66.1	65.5	64.8	63.0	5.83

During the period of twelve months, the loss of ascaridol was greatest when the oil was exposed to the direct heat and light of the sun (sample A). In diffuse but strong light of the laboratory there was also marked loss (sample D). Protected against light, the loss was much less (samples E and F) in the room with a varying temperature, while a constant temperature of 98.6°F. (37°C.) in the incubator did not prevent the loss, though the oil was kept in the dark (sample G).

The least amount of loss was noticed when the oil was kept in a temperature varying between 65°F. and 75°F. in subdued light (samples B and C).

The best way of storing oil of chenopodium thus appears to be in a cool place, where the temperature does not rise above 75°F., protected from direct light.

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BLOOD-PRESSURE VARIATION AND CARDIOVASCULAR CHANGES IN DIABETES MELLITUS*

By AMAL CHAKRAVARTI, M.B.

House Physician, Carmichael Hospital for Tropical Diseases, School of Tropical Medicine, Calcutta

THE rôle of diabetes mellitus in initiating or accelerating hypertension and arteriosclerosis has been engaging the attention of the profession for a long time, and numerous clinical studies have been made on the subject. In this paper observations on the blood-pressure variation and cardiovascular changes in fifty diabetic subjects are reported.

Out of 50 patients, 29 were admitted in the Carmichael Hospital for Tropical Diseases, and the remaining 21 were attending the diabetic clinic attached to the hospital. Forty-three were above the age of 40 and only 7 were females. The racial distribution of the patients was as follows:—

Hindu	20
Mohammedan	14
Jew	9
European or Anglo-Indian	6
Assamese	1

The majority of the patients had had the disease for five years or more. A few had complications: one came in with a hypertensive cerebral attack, one had a spreading ulcer over the left ankle, one had suffered from epidemic dropsy in the past, and three had associated infections, viz malaria, amœbiasis and a positive Wassermann.

(a) *Blood pressure.*—The blood-pressure readings of these 50 diabetic patients were compared with those of (i) 50 non-diabetic patients treated in the hospital for various tropical diseases. Very acute cases were left out and only those conforming in age and weight as far as practicable to the diabetic series, were chosen, and (ii) those of normal and healthy Indians given by Chopra *et al.* (1942).

From table I it is apparent that (i) the average systolic and diastolic pressures of young diabetic subjects show little variation from those of the non-diabetic or normal

* Paper rearranged by editor.

TABLE I

Showing average systolic and diastolic pressure in different age groups of both diabetic and non-diabetic patients compared to those of normal individuals

Age group	SYSTOLIC PRESSURES			DIASTOLIC PRESSURES		
	Diabetic patients	Non-diabetic patients	Normal men	Diabetic patients	Non-diabetic patients	Normal men
10-14	94.0	110.0	..	64.0	66.0	..
15-19	..	115.4	109.2	..	67.6	70.0
20-24	104.0	120.5	111.5	52.0	70.2	72.4
25-29	..	113.2	120.0	..	71.8	71.2
30-34	122.0	109.3	113.6	84.0	65.6	72.0
35-39	96.5	115.3	118.6	65.0	57.1	72.6
40-44	130.1	124.5	120.4	85.0	79.4	73.2
45-49	140.5	121.5	122.8	86.4	76.5	75.0
50-54	136.6	125.1	126.2	82.4	78.5	77.1
55-59	153.1	109.0	126.4	91.6	61.0	80.4
60-64	149.6	117.3	128.6	81.3	79.0	82.5
65-69	142.0	..	130.2	83.0	..	82.8
Mean for all ages.	126.8	116.4	118.7	71.5	70.2	72.3

series; after the age of 40, however, they are definitely higher than the normal or control figures, and (ii) the mean systolic pressure of diabetic patients for all ages is higher than normal. Moreover, taking systolic and diastolic pressures above 150 and 90 respectively as indicating hypertension, and below 100 and 70 as indicating hypotension, it is apparent that diabetics show a higher incidence of hypertension (38 per cent) against (12 per cent) in non-diabetics, and a lower incidence of hypotension (22 per cent) compared to 35 per cent of the non-diabetic group as will be seen from table II.

TABLE II

Showing percentage incidence of systolic pressures, hypertension and hypotension in diabetic and non-diabetic patients

Systolic blood pressure in mm. of Hg.

	Below 100	100- 140.	140- 150	150- 200	Above 200
Diabetic series ..	12%	56%	20%	20%	2%
Non-diabetic series	16%	80%	2%	2%	0%

'Hyper- tension'	'Hypo- tension'
(inclusive of diastolic pressure values)	
38%	22%
12%	35%

To ascertain whether the blood pressure showed any variation with clinical improvement and fall in the blood-sugar level, the in-patients were followed up. It was found that with improvement in the diabetic condition in young

patients, who are mostly hypotensive, the blood pressure gradually rises and comes up to normal, whereas in elderly patients with normal tension or hypertension, it remains unaltered or shows a tendency to rise.

Hypertension and diabetes.—Attempts have been made to show hypertension as a cause of diabetes. O'Hare observed that 11 out of 25 hypertensive subjects had low sugar tolerance and concluded that hypertensives have a pre-diabetic inclination. Several theories have been propounded, stating that hypertension by causing (i) an altered metabolism, (ii) hyperadrenia or (iii) arteriosclerosis in the pancreas may give rise to diabetes, but these have failed to stand the test of time.

Diabetes and hypertension.—A larger number of workers have viewed diabetes as a possible ætiological factor in the causation of hypertension. Their opinions are varied and may be grouped as follows:—

(i) Hypertension is not related to diabetes, and in cases of diabetes with hypertension some other co-existent factors are responsible (Rosenbloom, 1922; Adams, 1929; Wilder, 1939; and others). Schwartz (1936) holds that the frequent association of diabetes with hypertension is due to a higher incidence of diabetes in females who are very susceptible to hypertension, and in whom endocrine disturbances are very common, and that persistent hyperglycæmia as a cause can be ruled out. Barach (1942) observed that hypertension is related to body build.

(ii) Hypertension in diabetes is fairly common (Koopman, 1924; Major, 1929; Kramer, 1928; and others). The two diseases have been regarded as only stages of the same disorder (Kramer, 1928). O'Hare (1920) holds similar views.

(iii) Hypertension in diabetes is common, but young patients are mostly hypotensives (Joslin, 1923). The figures obtained for the incidence of hypertension in diabetes mellitus by different workers are given in the following table:—

	Per cent
Major	42.5
Kramer	39.0
Schwartz	30.4
Joslin	28.0
Katzklin (above 160 mm.) ..	25.0
Adams	21.9
In our series	38.0

(iv) The kidney has been incriminated as a cause by some, but nephritis is uncommon in diabetes, the true picture being one of nephrosis. Recently Allen (1941) has shown that the kidney lesion in diabetes is an intramural glomerulosclerosis with appreciable efferent arteriosclerosis, more common in patients with a widespread glomerular lesion, the constriction of the efferent arterioles probably playing an important rôle.

Diabetes and hypotension.—Hypotension has been mentioned by few and the cause is not clear; perhaps weakness of the heart muscle, due to slow fatty and glycogenic change and loss of body weight are responsible.

(b) *Arteriosclerosis.*—In our series of cases, a detailed study of the arteriosclerotic condition was not possible, but its extent was gauged from palpation of large superficial arteries. It was observed that arteriosclerosis in one or more of the arteries was present in 29 out of the 50 diabetics (58 per cent), 27 out of these 29 being elderly subjects. In 3, the arteries could not be palpated on account of excessive obesity, and in 18 arteriosclerosis was absent.

Of the patients with superficial arteriosclerosis, the majority had albumen in the urine, some complained of defective vision, and 7 had slight cardiac symptoms. These had probably some degree of internal sclerosis.

(c) *Heart.*—Only 7 patients presented cardiac symptoms. Of these, 3 complained of a feeling of breathlessness on exertion, 2 of occasional palpitation, 1 of palpitation and giddiness and gave history of anginal attack. Examination of the heart, however, revealed no serious defect except that in 5 patients the heart was slightly enlarged outward, and in the patient with anginal history and hypertension the enlargement was considerable.

Friedman (1935) found cardiac hypertrophy in 47 per cent of cases and in only 18 per cent of these was the enlargement more than slight. Quoting Cabbot's figures of cardiac hypertrophy (39 per cent) in diabetic arteriosclerotic patients, he concluded that cardiac hypertrophy in diabetes cannot be considered of any special significance. In his (Friedman's) series, 19 per cent had cardiac symptoms and only 9 out of 129 patients had anginal attacks. The same view is held by others. In Hepburn and Graham (1928) series, 56 patients out of

123 had an abnormal electrocardiogram at the beginning of treatment and at the end of treatment 15 returned to normal. Unless severe arteriosclerosis is present, the condition would thus seem to be reversible.

Summary

1. Blood-pressure variation and cardiovascular changes in 50 diabetic patients have been studied.

2. It was observed that hypertension and arteriosclerosis are of common occurrence in elderly diabetics; young patients usually manifest low pressures and with early and successful treatment they are likely to regain their normal tension.

3. Cardiac abnormalities are infrequent in diabetes.

Acknowledgments

The writer expresses his gratefulness to Dr. J. P. Bose, Physician in charge, Diabetes Department, for his valuable suggestions and encouragement, and to Drs. S. C. Panja, S. Bose, and A. Hossain (colleagues), for their help in carrying out the study.

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MYOTONIA CONGENITA

(THOMSEN'S DISEASE)

By AMIR CHAND, F.R.C.P.E.

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and

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 MAJOR, I.M.S./I.A.M.C.

No record of this rare condition can be traced in India.

The main characteristic feature of this heredo-familial disease of childhood is the involuntary persistence of muscular contraction when the initiating stimulus, voluntary, electrical or mechanical, has ceased. The muscular contraction is slow and tonic. Its retarded relaxation leads to characteristic clinical features. The child is left sitting when others run away. A yawn becomes drawn out because the mouth

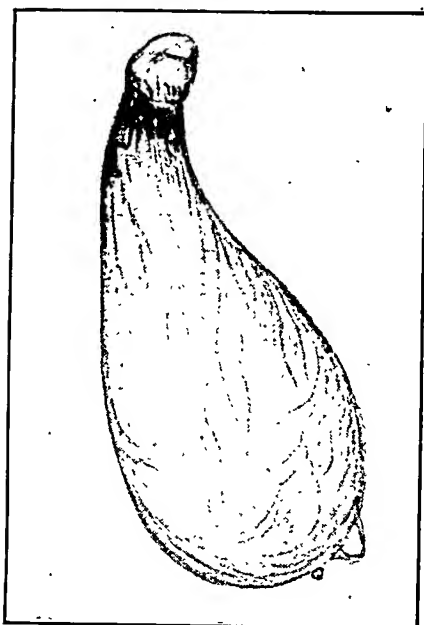


Fig. 1.—Papilloma on the fundus of the gall-bladder.

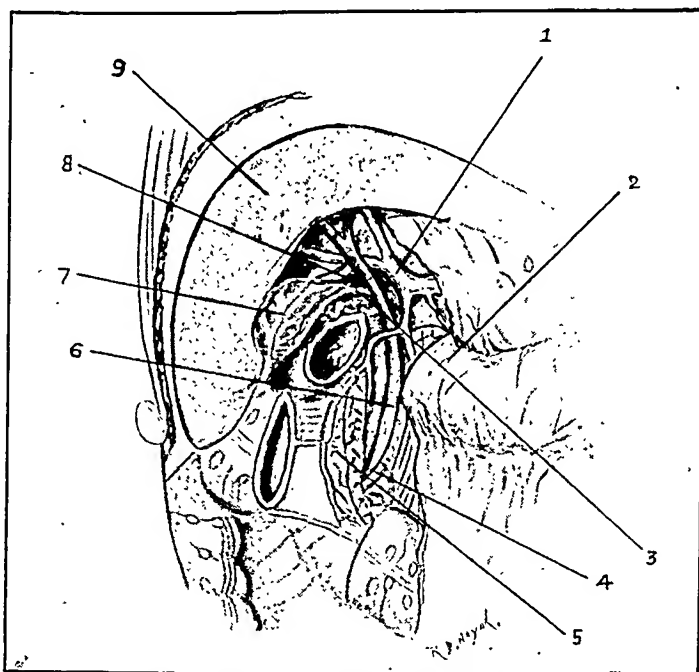


Fig. 2.—Aberrant branch of hepatic artery.



Fig. 3.—Gall-bladder buried in the liver.

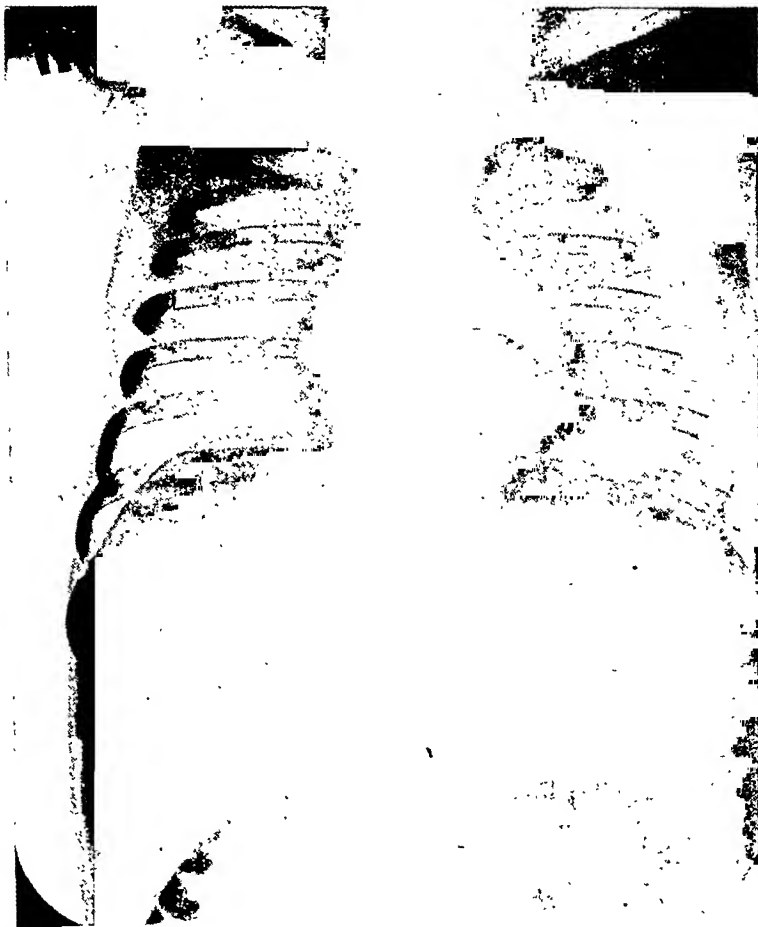


Fig. 4.—Absence of cystic duct.



PLATE XIII

CONGENITAL HEART DISEASE IN A CASE OF 'RESISTANT'
KALA-AZAR WITH PULMONARY TUBERCULOSIS : AMAL
CHAKRAVARTI. PAGE 351.



Skiagram of chest showing globular heart with increased width of cardiac shadow situated in mid position; scattered areas of mottling in both upper lobes; calcified hilar glands.

cannot be shut quickly. Even trivial upsets of equilibrium, which would be quickly righted in normal individuals, lead to falls in affected persons because the correcting muscles cannot be called into play in time. The defect often tends to lessen temporarily after exercise. Myotonia may be generalized throughout the voluntary musculature or may be restricted to sets of muscles.

The cause of the disease is not known. Russell and Stedman (1936) showed that acetylcholine, prostigmin and potassium increased the defect. Kennedy and Wolf (1937) showed that quinine reduced the disability. This would suggest that the neuromuscular junction is the site of the lesion. Brown and Harvey (1939) on the other hand indicated the probability of a primary muscular disorder. The abnormal muscular sensitivity to direct mechanical stimulation (e.g. by a tap) remains unaffected by curare or degeneration of motor nerve endings. This experimental work has been carried out in America on a strain of goats suffering from myotonia indistinguishable from the human variety.

Quinine has given good therapeutic results in both man and goat.

Case report

A. D., Punjabi male, 16 years old, a vegetable seller, was seen in December 1938, at the Mayo Hospital, Lahore, with complaints of generalized stiffness of both extremities improving slightly after exercise, and inability to lift the basket of vegetables from the ground on to his head.

His history extended to childhood and infancy when he was noticed to be 'weaker' on his legs than the normal child of his age, although he looked quite strong. The disease now constituted an economic handicap as he was unable to carry the vegetable basket.

Relatives could not be examined, but the parents and the two younger sisters were stated to be fit, and no one else in the family was known to have suffered from a similar disability.

The patient was a well-built boy with an apparently good general muscular development. His central and peripheral nervous systems were normal except for a marked nystagmus in all directions. This in the absence of any other abnormality was considered to be congenital in origin. All muscles, particularly those of the limbs, were hypertrophied and the muscle tone was increased. There was no rigidity. The patient could not relax or tighten his grip quickly, but this improved after several attempts. He was unable to get up suddenly and run. When asked to do so, he performed the actions slowly and started running slowly only after covering about five to ten yards at an increasing walking pace. Regarding the difficulty of lifting his vegetable basket on to his head, he could not jerk it up after he had raised it from the ground slowly but quite easily.

Stools, urine and blood picture were normal except for an eosinophil count of 735 per c.mm. for which no cause could be found. The total white cell count was 6,250 cells per c.mm. The Wassermann reaction was negative.

Treatment with fifteen grains of quinine daily resulted in marked subjective improvement but no appreciable diminution of myotonia could be demonstrated after ten days' therapy.

The clinical picture was thus typical of the disease, and a correct out-patient diagnosis was

made by the physician admitting the patient. The nystagmus and the eosinophilia were unusual features. The only other disease which has to be borne in mind for differential diagnosis, dystrophia myotonia is easily distinguished by the characteristic associated muscular wasting, cataract and testicular atrophy. The familial character in this case could not be ruled out in view of an unreliable history and the absence of examination of relatives. Mendelian inheritance of the defect is the rule, though sporadic cases are known to occur rarely.

Summary

A case of *Myotonia congenita* with eosinophilia and congenital nystagmus is reported. The condition is believed to be unrecorded in India so far. The salient features of the disease are described.

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A Mirror of Hospital Practice

CONGENITAL HEART DISEASE IN A CASE OF 'RESISTANT' KALA-AZAR WITH PULMONARY TUBERCULOSIS

By AMAL CHAKRAVARTI, M.B.

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CASES of kala-azar with a combination of congenital heart disease and pulmonary tuberculosis are not on record. The following is a case report.

A Hindu male child, 8 years old, was admitted to the Carmichael Hospital for Tropical Diseases, on 23rd October, 1944, with a history of repeated febrile attacks, for two years. Diagnosed and treated outside as a case of kala-azar with different antimonials, a total dose of 1.65 grammes was given in 32 bi-weekly injections. The treatment did not control the fever.

History.—The mother had very often noticed the child getting 'blue' during fits of crying or coughing and out of breath at times. The patient had 9 brothers and sisters; 6 died in their early infancy, 5 within a fortnight of birth and one at the age of 6; all were prone to get 'blue'.

Condition on admission.—The child was pale and anæmic; normal growth; no developmental anomaly; no cyanosis. Fingers showed slight clubbing; ankles slightly cedematous; carotid pulsation noticeable; temperature 101.4°F., pulse rate 120 and respiration 25 per minute. The patient practises mouth breathing. Liver enlarged to 2 fingers and spleen 6 fingers below the costal margin. Nothing abnormal detected in the lungs.

Heart—the apex beat half an inch outside the mid-clavicular line in the left 4th intercostal space. In addition, two other pulsations were visible: (1) in the

second left interspace, probably arising in the pulmonary artery, and (2) in the epigastrium, well palpated under the left costal margin suggestive of right ventricular dilatation. Percussion: an enlarged heart situated in normal position. Auscultation: a loud, harsh systolic murmur towards the base of the heart, in a localized area with the point of maximum intensity in the 3rd interspace, just outside the left sternal border; no conduction along the vessels of the neck. Pulmonary second sound slightly diminished in intensity. Blood pressure 82/52 (right arm), 80/55 (left arm).

Laboratory findings.—Antimony and aldehyde tests were positive, and spleen puncture showed *L. donovani* bodies in fair numbers. Urine—no abnormality; stools—giardia cysts. Repeated examinations of sputum—no acid-fast bacillus seen. The blood counts were as follows:—

Date	Hæmoglobin	R.B.C.	C.V.	M.C.V.	M.C.H.	M.C.Hc.	W.B.C.
25-10-44	35% (4.76 gm.)	1.63	15.5	95.09	28.6	28.6	1,500
2-1-45	62% (8.25 gm.)	3.02	25.5	84.4	27.3	32.3	4,300

A skiagram of the chest taken on 1st December, 1944, revealed (1) a globular heart with increased width of the cardiac shadow situated in the midposition, (2) scattered areas of mottling in both upper lobes and calcified hilar glands, suggestive of early pulmonary tuberculosis (see figure, plate XIII).

On fluoroscopy a globular heart with the right and left borders extending beyond the median line and presenting synchronous systolic contractions; the apex appeared rounded and displaced outwards, the vascular curves normal; retro-cardiac space free.

Electrocardiogram.—Heart rate 107 per minute; sinus tachycardia. P upright in all leads; marked left axis deviation.

Treatment and progress.—As the patient was resistant to antimony, he was put on M.&B. 736 (phenamidine) of which he had 3 courses, the total dose being 1.57 gm. This was followed by a course of M.&B. 744 (stilbamidine), and he also had symptomatic treatment for cough, anæmia, etc.

His pyrexia was now controlled and the anæmia definitely improved. The spleen was also diminished in size, and he gained 14 pounds in weight.

Discussion

The cardiac lesion in this case apparently belongs to the 'cyanose tardive' variety of congenital heart disease in which cyanosis is not a constant feature but appears temporarily or as a terminal phenomenon, when a reversal of flow is effected in the arterio-venous shunt. This is likely to happen when through a septal defect too much venous blood gets transferred into the left ventricle.

The loud and harsh systolic murmur in the left third space, synchronous bulging of both borders of the heart, absence of high P wave, and marked left axis deviation point to the condition being due to a defective interventricular septum (Roger's disease) and not to the auricular septal defect in which the systolic murmur is

usually faint, and audible, if at all, in the second left interspace, cyanosis is a late manifestation, the pulmonary second sound is usually accentuated and the aorta is hypoplastic; and the electrocardiogram generally shows high P waves and right axis deviation.

The early tuberculous infiltration of the upper lobes of both lungs did not flare up with diamidine treatment; on the other hand, it showed definite improvement.

I express my thanks to Dr. P. C. Sen Gupta for his permission to report the case and for his valuable suggestions.

THE USE OF THE FEMORAL VEIN FOR VENOCLYSIS

By D. R. VAIDYA, M.S., B.M.S.
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MANY a time a surgeon is at a loss as to what to do in a case of shock because of the difficulty of getting a needle into a superficial vein. The fluid is there, e.g. plasma, whole blood, saline, etc., but the veins are all collapsed, and repeated attempts to get a needle into a vein now fail.

We have found at such time the following method very useful. It has never failed until now. In no less than 20 cases we administered the fluids by this method.

The technique is very simple. Palpate the femoral artery of the patient just at Poupart's ligament. About $\frac{1}{2}$ to $\frac{1}{4}$ inch medial to the artery runs the femoral vein. Press lightly above the inguinal ligament in order that the femoral vein may become distended. Take a transfusion needle and insert it at a point $\frac{3}{4}$ inch below Poupart's ligament and $\frac{1}{4}$ inch medial to the femoral artery gently pointing upwards, outwards and backwards. One must remember that the vein is situated at this point fairly deep (about 1 inch) and on entering it one experiences the same feel of loss of resistance as one does in puncturing a superficial vein.

The technique was suggested by my chief Dr. K. C. Gharpure, M.S., F.R.C.S.E.

The following are the advantages of this method.

- (1) The femoral vein is a large vein and in case of even collapse, is wide enough for a big transfusion needle.
- (2) Unnecessary dissection of a vein is prevented.
- (3) No special apparatus is necessary.
- (4) Difficulty due to reflex veno-spasm due to trauma in opening a small vein is obviated.

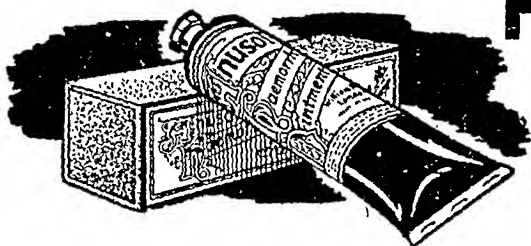
The only disadvantage is the fear of puncturing of femoral artery. If the artery is punctured it can be made out by the spurting of blood. Just remove the needle and nothing is lost.

I have to thank Colonel S. R. Prall, I.M.S., and Dr. K. C. Gharpure, M.S., F.R.C.S.E., for allowing me to publish this and for their interest in my work.

CORRIGENDA. In the article on 'Weight, height and chest measurements, etc.' by Dr. M. G. Kini in our June number—

On page 301, para 3, line 7—for 'height + chest girth' read 'height × chest girth'.

On page 302, under figure 1, A—for 'lumbar view' read 'lumbar curve'.



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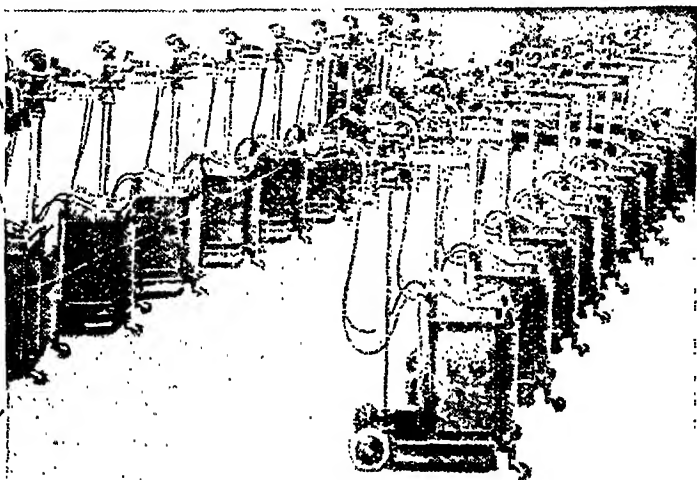
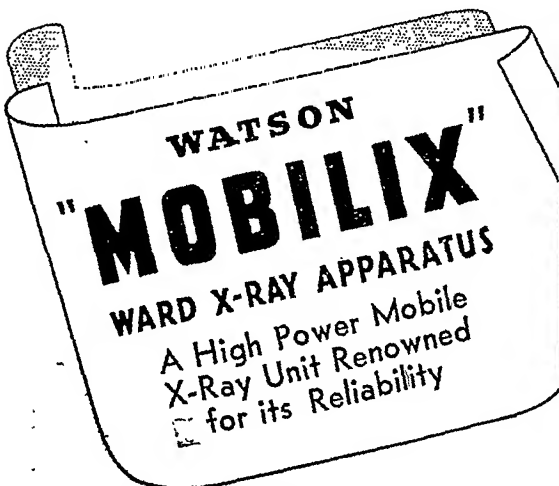
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Indian Medical Gazette

JULY

WOUND SHOCK

THE war has widened our conception of shock, which is now regarded as a complex state resulting from multiplicity of causes, but most often from hæmorrhage. Its essential feature is failure of the circulation, and this may appear immediately or soon after injury, or may be manifest at a later stage from various causes such as plasma loss as in burns, fat embolism, peritonitis and gas gangrene. Two or more of these conditions may be present in the same patient, producing a complicated clinical picture. Thus a man may have a severe fracture of the thigh followed by pulmonary fat embolism and later gas gangrene; each of these states may induce a state of shock. The mechanisms which bring about this circulatory failure are still not well understood, but they seem to vary in different types of injuries. One form of shock—vasovagal collapse, a condition characterized by a slow pulse and a fall of blood pressure due to dilatation of muscle arterioles—may follow psychic or painful stimuli with or without any loss of blood, and indeed it may occur in susceptible individuals after the most trivial injuries. Thus it is seen that shock is not a single entity but, as emphasized by the Medical Research Council (1944), a non-specific syndrome of great complexity. One of the best understood factors in the production of shock is acute reduction of the blood volume—oligæmia, and this commonly occurs in severe wounds from loss of blood externally or into the traumatized area. We shall here deal with certain aspects of diagnosis and treatment in this type of shock.

It is easy to recognize shock when once it is established. The patient looks pale, with a cold, sweating skin and sub-normal temperature; mentally he is clear, but may be restless with a touch of anxiety, and even if badly wounded, he does not complain of much pain. He has an intense thirst, but may vomit shortly after each drink. The blood pressure is low, and the pulse is weak and rapid, and may be almost imperceptible; sometimes there is air-hunger which means impending death. Such a picture is unmistakable, and denotes profound collapse of the circulation, calling for immediate appropriate treatment. But in the early stages, clinical appearances may be deceptive. There is a tendency to diagnose shock only when the blood pressure is low, but even after considerable blood loss it may be as high as 150 mm. of Hg. or even more. It seems that there is a phase of vaso-constriction which keeps up the failing peripheral circulation; the patient may

recover without special treatment, or may pass suddenly into a state of profound shock. Hence no reliance should be placed upon a single blood pressure reading, but it should be taken frequently, especially before and during an operation. In some patients the pulse remains slow, and the sub-normal temperature which is one of the most constant signs is not always coincident with the fall in blood pressure. So for early diagnosis we must depend on a general appreciation of the clinical picture. To quote Zachary Cope (1944), 'shock may be indicated by a sub-normal temperature with a low blood pressure, although the pulse rate may be within normal limits. Or it may reveal itself by pallor, sweating, sub-normal temperature and a small rapid pulse, while the blood pressure may remain approximately normal. And there are also cases in which the appearance and mental condition give no indication of the serious state of the circulation which the sphygmomanometer may demonstrate'. For practical purposes, the best guide is the severity of the injuries. If the dressings, clothing or blankets are grossly blood-stained, if there is much swelling around the wound, or if the total area of the wound is large with much laceration of tissue, then one may assume that shock will develop sooner or later. Of course, there may not be much blood visible in case of internal bleeding. It is worth remembering that in a closed fracture of the femur there may be as much as two pints of blood extravasated in the muscles near about the injured part, and that serious shock may appear even after small bleeding. In a hypertensive subject the blood pressure may appear normal though in fact it has fallen considerably.

The treatment of wound shock consists in replacement of lost blood by transfusion combined with efficient control of bleeding for which large pressure dressings are preferable to tourniquets. If it is an injured limb, a splint is put on, otherwise for the time being no local treatment is attempted. Broadly speaking the indications for transfusion are: (i) when the systolic blood pressure is below 90 mm. of Hg. and the pulse is rapid, (ii) when there is evidence of severe blood loss or severe wounding with laceration, even if there is little reduction of systolic pressure, (iii) in doubtful cases it is better to give than to withhold transfusion. Blood is the fluid of choice for massive transfusions, but plasma or serum is as efficacious as blood in the initial stages of resuscitation. Its advantage is that it can be used without any typing or cross-matching, but it is not safe to give more than two pints owing to the hæmo-dilution which makes it less effective and the intractable secondary anæmia that follows in two or three weeks' time. The amount required depends on the response of the patient. On an average it is three or four pints, but additional amounts may be required during and after operation. The fluid may be given as rapidly as it will run under gravity until the

blood pressure has risen to over 100 mm. Hg., when it may be reduced to a drip. To be effective, transfusion must be given as early as possible. If the blood pressure has been low for several hours, it may fail to have any effect owing to the 'irreversible state' probably caused by damage to the capillaries and vital centres, but sometimes remarkable recoveries from prolonged circulatory failure have followed transfusion, so it should never be withheld even in desperate cases. In assessing recovery, several blood pressure records are the most useful guide, but other clinical details and subjective improvement must be considered. Unsatisfactory response is often due to continued or recurrent bleeding, or as just mentioned, to the irreversible state, when fast and larger transfusions may be necessary; a rate of a pint in five minutes may be obtained by applying pressure from a Higginson's syringe connected to the inlet tube of the transfusion bottle. Transfusion is useless in brain damage and bacterial infections, especially gas gangrene and peritonitis, and dangerous when pulmonary complications are present. The sooner the patient is operated on after resuscitation, the better, or he may relapse into shock. Relapse however occurs more frequently during and after operation if the blood volume had not been made good, or falls again from slow blood loss. But, as Professor Wilson (1944) points out, relapse can occur even when the blood volume has been completely restored. Successful resuscitation before operation does not mean that the condition is again normal; still less is it a guarantee of eventual recovery. The man who has been rescued from severe shock remains in a precarious state, abnormally sensitive to blood loss and to the toxic action of anaesthetics.

Some of the other measures for the treatment of shock need a few remarks. Body heat should be conserved by the application of warmth, but not to such an extent as to produce or increase sweating. Overheating, *e.g.* by electric cradle, is not only harmful but dangerous. Oxygen is not helpful. Morphine is given, though not as a routine, for the relief of pain and apprehension; $1/6$ grain given intravenously is usually satisfactory and may conveniently be given with the transfusion fluid. Several cases of morphine poisoning have occurred from repeated subcutaneous injections, the large total dose being subsequently carried into the circulation as the latter improved. Dehydration is often present and requires attention. Immobilization of limbs, especially if there are fractures, and gentle handling are essential. Shocked patients do not stand long journeys well. They should be lifted and moved as little as possible, and taken from the ward to the theatre in a bed and not on a trolley. At operation the essentials are wound excision, removal of damaged tissue, hæmostasis and gentle handling of tissues. Administration of anaesthetics needs good judgment and care. Deep anaesthesia itself is a state

of shock. Whichever is chosen, it should be given with due regard to the depression of the patient and only in sufficient quantity to produce the requisite effect. Shocked patients never require the same amount as a normal person. Spinal anaesthesia is never used. There may be considerable fall in blood pressure as the combined result of operation and anaesthesia, but patients usually recover without transfusion.

It is unnecessary to add that post-operative care is equally important. The patient remains ill for several days and is apt to get new complications, chiefly as the result of bacterial infection. The treatment of shock indeed requires continuous and assiduous attention until convalescence sets in.

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R. N. C.

THE SULPHONAMIDES IN BACILLARY DYSENTERY

THE value of this group of drugs in bacillary dysentery is now universally recognized, and in the opinion of many it can replace all other forms of treatment such as antidysenteric serum, bacteriophage, etc. There are some workers who still believe that these other preparations may have a rôle in bacillary dysentery, but possibly a subsidiary one. The vast majority of cases of bacillary dysentery respond very well to the sulphonamides.

It has been considered that the effectiveness of the sulphonamides depended on the concentration obtained in the gut, and that poorly-absorbed sulphonamides, such as sulphaguanidine and succinyl sulphathiazole, are the drugs of choice in bacillary dysentery; being absorbed slowly from the gut, they rarely produce any toxic symptoms. Some workers have now diverged somewhat from this view. It has been reported that, particularly when the gut is ulcerated, a considerable amount of these drugs may be absorbed, sufficient sometimes to produce blockage of the ureters on excretion. Moreover, several workers have found that sulphathiazole which is cheaper and readily available, in spite of its relatively high absorption, gives results at least equal to those obtained with sulphaguanidine. Moreover, these drugs (sulphaguanidine and sulphasuccidine) are not very effective against Sonne dysentery. Various workers have therefore been trying to discover still more effective sulphonamide drugs in bacillary dysentery. One of the drugs tested is sulphanilyl benzamide.

Sulphanilyl benzamide was suggested for use in dysentery by Brownlee and Tonkin in 1941 particularly in the treatment of Sonne infection.

These infections are usually mild, but it has been found that the carrier state may be persistent for several weeks. In February 1945 Swyer and Yang reported favourable results in the treatment of Sonne dysentery with this preparation. Sulphanilyl benzamide was apparently first produced and tried *in vitro* and in animals at the Wellcome Physiological Research Laboratory, Dagenham, England.

In our June number we published an article by Bose and Ghosh on 'Sulphanilyl benzamide in the treatment of bacillary dysentery', and in our present number we publish an article by Bose, Sen Gupta and Basu discussing the use of this drug in bacillary dysentery, describing its low toxicity in animals and quoting the report of Swyer and Yang in its effectiveness in man even in Sonne dysentery.

We think that this paper, in making out a case for sulphanilyl benzamide, tends perhaps to exaggerate the toxicity of sulphaguanidine and also to minimize the value of sulphathiazole in bacillary dysentery. It talks about the 'inactivity of sulphathiazole *in vivo*'; this is not in agreement with reports of several recent workers; sulphathiazole has been widely used in the treatment of bacillary dysentery with excellent results.

If it is confirmed that sulphanilyl benzamide is more effective in Sonne dysentery cases than the other sulphonamides, and if it has no drawbacks, it may become the drug of choice in bacillary dysentery. It should, however, be pointed out that Sonne dysentery forms a small proportion of the total number of cases seen.

J. L.

Medical News

INDIAN CHEMICAL MANUFACTURERS' ASSOCIATION

A PRESS communique states that the Government of India have agreed to give facilities to the Indian Chemical Manufacturers' Association to send a delegation to the United Kingdom and the United States of America with a view to studying the latest developments in the chemical industries in those countries. The delegation would consist of about ten representatives of most of the prominent chemical concerns all over the country who are in the membership of the Association. The delegation is expected to leave for the United Kingdom sometime in the beginning of August.

CAN EPIDEMICS OF MALARIA BE FORECAST?

SINCE 1922 the Punjab Public Health Department have been issuing annual forecasts regarding the probability of the occurrence of malaria in an epidemic form in different parts of the province. These forecasts have been found to be reasonably accurate, and an improved method is now being worked out. From a study of malaria during the last 77 years, it appears that in the Punjab epidemics tend to occur after a period of 5 years, but this periodicity has not yet been

conclusively established. The relationship between rainfall and malaria is also being studied in detail.

COMMONWEALTH OF AUSTRALIA SERUM LABORATORY

FOUNDED on a small scale in 1915 when the first world war threatened to cut off Australia from overseas supplies, these laboratories have grown steadily and are an example of successful government enterprise, being self-supporting and even showing profit for many years. Sera, vaccines, penicillin and other biological products are manufactured and research work is carried on. During the present war, they have supplied their products to the various services and for the civil needs of various countries including India and China.

ABSORPTION OF AEROSOL PENICILLIN VIA THE LUNGS

(The *Lancet*, 14th April, 1945, p. 468)

IN a preliminary communication Knott and Clark say that aqueous sodium penicillin remains active for a considerable time when dispersed as an aerosol. Penicillin inspired in this form, without the use of a mask, readily passes into the circulation, is excreted in the urine, and can soon be detected in the blood in therapeutically useful concentration. It is suggested that the administration of penicillin by this means may have several useful clinical applications.

THE NOMENCLATURE OF B.P. AND OTHER DRUGS

(The *Pharmaceutical Journal*, 14th April, 1945, p. 191)

At a meeting of the Western Pharmacists' Association, England, T. D. Whittet, Ph.C., made the following remarks:—

Multiplicity of trade names for definite chemical substances is the cause of considerable confusion to both physician and pharmacist, and leads to much needless expense and duplication of stock. For example, procaine hydrochloride is issued under at least thirteen different trade names, while there are over fifty different synonyms for sulphanilamide. In the latter case many of the firms engaged in this trade buy sulphanilamide from the common source and merely pack and label it independently. The sole object here is obviously to make a profit, and not to fulfil a consumer need, for when a drug is sold under a proprietary name, it costs on an average three times as much as when sold under an official name.

There are over sixty different barbiturate derivatives, many of them having no advantage over the official barbiturates and differing little from them in chemical constitution. Here, instead of giving a 'fancy name' to the same drug, some manufacturers have produced various closely related compounds with the main object of their being different from the drugs of another firm.

When one considers the great advances in medicine in recent years and the large number of genuine new drugs, it is little wonder that the busy doctor has no time to memorize a long list of synonyms for simple drugs, and as the *British Medical Journal* stated recently, 'the practising doctor cannot be expected to know more than one name for a drug, and knowledge of a single name ought to be sufficient to permit him to identify a drug even when several different brands are on the market'.

In America, conditions are much more satisfactory, for the Council on Pharmacy and Chemistry of the American Medical Association refuses to recognize proprietary names for articles which are included in their Pharmacopœia or National Formulary. The work of this Council should be an example to us in Britain of what can be done to discriminate between genuine and spurious remedies.

Public Health Section

CONTROL OF ACUTE BACTERIAL
RESPIRATORY DISEASES BY
SULPHA-DRUGS*

By J. N. BERRY, M.D.

RESPIRATORY diseases account for a large part of morbidity both in children and in adults. Various methods have been used and advocated for the control of droplet infection in institutions, including elimination and proper treatment of throat carriers of *Streptococcus hæmolyticus*, use of flannelette masks and gowns by the nursing staff, proper spacing of beds (Doyle and Robertson, 1944), and providing separate cubicles in the case of children (Jacoby, 1944). The application of dust-laying oils to the hospital bed clothes (Harwood, Powney and Edwards, 1944) and oiling of the floors (Anderson, Buchanan and MacPartland, 1944) or wet mopping in place of sweeping (Doyle and Robertson, 1944) are said to reduce the bacterial content of air and in consequence cut down the spread of air-borne infection. Other methods have aimed at sterilization of the air by ultra-violet radiation or hypochloride sprays or prophylene glycol vapour spray (Picken, 1944).

Most of the acute respiratory tract diseases are caused by Gram-positive cocci which are very susceptible to treatment with sulpha-drugs. Recently, these have been used on an extensive scale for prophylactic control in the American Army and the reports are very encouraging. Holbrook (1944) gives results of up to 75 per cent reduction in the incidence of respiratory diseases, streptococcal infections and rheumatic fever by the use of sulphadiazine prophylaxis on a large troop population (9,000). Thomas (1944) advocates 1 gramme daily doses of sulphadiazine for a period of 5 years to prevent recurrence of rheumatic fever. For 4 years, from October or November to June, he gave 1 to 1.2 gramme a day of sulphanilamide to a group of adolescents and young adults and compared the results with those observed in an untreated control group of similar rheumatic subjects. The results both as regards inhibiting beta-hæmolytic streptococcus infections and preventing rheumatic recrudescences were strikingly favourable. During these 4 years not a single major attack of rheumatic fever occurred in any patient while taking sulphanilamide prophylactically. Warren (1944) reports a marked reduction in the number of attendances at the out-patient department and hospital admissions after the use of 1 gramme daily of

sulphadiazine among 9,000 soldiers. The most effective reduction was in diseases caused by beta-hæmolytic streptococcus, scarlet fever and naso-pharyngitis due to streptococci.

Even more striking than these have been the results of Coburn (1944) in U.S. Navy. Prophylactic sulphadiazine, usually 1 gramme a day, was administered to part of the personnel in several training centres from December 1943 to March 1944, with other groups at the same centres serving as controls; about 250,000 men were taking the prophylactic medication, and an equal number were observed as controls. During this period, hospitalization for severe respiratory diseases was reduced by 80 to 90 per cent, streptococcal infections were reduced by 85 per cent, and the incidence of rheumatic fever dropped equally sharply so that in one centre there was only one case among the treated group to every 14 cases among the controls. The attack rate of rheumatic fever decreased gradually over the course of several weeks, indicating that prophylactic sulphadiazine interferes with the development of acute rheumatic fever by preventing the antecedent streptococcal infections. In a preliminary report summarizing his observations on 30,000 men, he concludes that the continuous ingestion of 1 gramme of sulphadiazine daily is adequate (a) to check a well-advanced streptococcal epidemic, (b) to check a streptococcal outbreak at its onset, and (c) to protect 85 per cent of susceptible recruits from implantation with bacterial respiratory pathogens.

The optimum dose.—In adults, Holbrook (1944) found 1 gramme of sulphadiazine daily the most effective dose, but he also obtained 'almost identical satisfactory results by the use of 0.5 gramme daily'. Coburn (1944) found 0.5 gramme a day 85 per cent effective but Thomas (1944) concludes that 0.5 gramme a day is slightly less effective than 1 gramme a day in adults.

Toxic reactions and dangers.—Lee (1944), on giving a single dose of 2 grammes of sulphadiazine to 25,000 persons, observed 13 severe reactions, 3 of them being critically ill. In these cases there was a history of previous reactions with sulphonamide, and the elimination of such cases from the mass prophylactic programme greatly diminished the incidence of severe reactions. None of them died. Holbrook (1944) reports that out of 40,000 troops given 1 gramme of sulphadiazine for 3 months, 13 individuals only lost some days off duty and 33 had mild manifestations not resulting in loss of time on duty. There were no deaths, no renal complications and no evidence of neutrophil leukopenia. The major disabilities were skin lesions occurring between the 1st and 16th days of the administration of the drug. These disappeared when

*The American work which is quoted in this article is not supported by British experience, a summary of which appears in this issue under Current Topics (page 363). Further investigations are required under well-controlled conditions.—Editor; I.M.G.

the drug was discontinued. In the only two individuals who developed high febrile reactions, there was a history of previous sulphonamide reactions. Coburn (1944) in his 30,000 navy trainees had severe drug reactions in only one in 10,000 individuals, and these reactions were equally divided between granulocytopenia and exfoliative dermatitis.

Maintenance of the patients in the best possible physical condition, a gradual increase of dose from 0.5 gramme to 1.0 gramme a day in a period of three weeks, immediate reports of any rash or sore throat to the physician, frequent hæmoglobin estimations and total leucocyte counts, and elimination of those with previous history of severe reactions with sulphadiazine will tend to minimize the incidence of untoward reactions. The possibility of development of drug-fast respiratory pathogens is very remote and unlikely (Coburn, 1944). The possibility of individuals becoming sensitized to the drug on a mass scale has been considered, but repeated periods of prophylaxis on the same groups have failed to demonstrate any developing sensitivity (Holbrook, 1944).

The choice of drug.—Sulphadiazine has been the most extensively used drug in mass prophylaxis programmes. Thomas (1944) and also Feldt (1944) used sulphanilamide for prophylaxis against rheumatic recurrences, and the latter recommends it as a safe and effective measure, but the rapid absorption and gradual elimination of sulphamerazine which make possible the maintenance of a concentration in blood higher than that with sulphadiazine (Welch *et al.*, 1944) or any other member of the series, may make it (sulphamerazine) the drug of choice in the future. In our country, sulphanilamide, because of its cheapness, easy availability and the absence of serious renal complications, may be the most used drug for a long time to come.

Observations

A high incidence of respiratory infections was observed in the crèche of a cotton mill. This crèche caters for 28 babies, all under 2 years, and is under the supervision of one trained nurse and 2 *ayas*. The babies are housed in a single room 45 by 22½ by 11½ feet. The cradles are in 3 rows, 6 feet apart, and are spaced from each other at 1 foot distance. The children come from poor labour class, whose housing conditions are far from hygienic, but their nutrition in general is satisfactory. Mothers are allowed 45 minutes' rest period 3 times a day (10 working hours) to feed them. All infants above one year of age are given two additional feeds of 5 oz. milk and one feed of wheat porridge in between the two. The weight of each child is taken fortnightly and charted. Any illness during the period of stay in the crèche is also charted on a graph.

During a period of observation extending from 11th November to 31st December, 11 cases

of acute respiratory infection were recorded in the 28 babies (an incidence of 39 per cent). There were 4 cases of otitis media, 4 of bronchopneumonia, one of lobar pneumonia and 2 of acute naso-pharyngitis. Four of these occurred in November and the remaining 7 in December. As none of the other methods to check the further spread of infection was possible due to local conditions, prophylaxis by sulphonamides was the method of choice. One-fourth of a tablet (0.125 gramme) of sulphanilamide was given to all the babies except two who were under three months of age and who were given ½ of a tablet a day. This was continued for two months, from 1st January to 28th February by which time the winter season ended. The results were highly satisfactory. No case of severe respiratory disease occurred during this period. Two or three babies had common cold but none of the usual sequelæ due to bacterial super-infection developed. The only cases of illness during the period were two cases of P.U.O. (presumably malaria) in previously known malarious children and which yielded promptly to quinine administration. Thus an incidence of 25 per cent in December (7 cases among 28 babies) was reduced to nil in January and February by the daily use of a small dose of sulphanilamide. No toxic reactions were observed in this small series.

Conclusions

Small daily doses of sulphonamides are a safe and effective method for the control of acute bacterial respiratory diseases as well as for preventing recurrences of rheumatic fever. It may be the method of choice in a small institution while it is the only practicable method for large-scale application.

Acknowledgment

My grateful acknowledgments are due to Mr. G. S. Nevatia, the Secretary of the Pulgaon Cotton Mills, Pulgaon, for allowing me to carry out the sulphanilamide prophylaxis in the mill crèche and for permission to publish this paper.

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SOME OBSERVATIONS ON FLY BREEDING IN COMPOST TRENCHES*

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Introduction

THE usual two types of town wastes, viz. rubbish (*katchra*) and night-soil, are dealt with separately in their sanitary disposal. In most municipal towns in this province, *katchra* is stacked in heaps above ground, and near the outskirts of the town. Our observations have shown that it is as much a source of fly nuisance as the night-soil, but very little attention is paid to its sanitary disposal. Night-soil usually is buried in shallow or deep trenches under a six-inch or one-foot layer of earth. It has been observed that unless this is done carefully, smell nuisance and prolific fly breeding are common features of trenching grounds. As the night-soil by itself undergoes only a mesophilic fermentation, fly eggs and maggots, with which it is invariably infested, are not killed for lack of rise of temperature to a lethal point.

These old methods of disposal could be replaced by the compost method which has proved to be of higher sanitary standard, and leads to better utilization of town wastes as manure. The agricultural value of town waste as organic manure is considerable if properly exploited. The methods in vogue are, however, wasteful. *Katchra* or rubbish is in some places directly applied to fallow-lands which are put under vegetables when the refuse is completely decomposed. In many towns it is usually wasted. The trenched night-soil is generally not sold as manure for the following reasons: (1) A very large quantity of earth is carried away from the trenching ground when the night-soil manure is sold. In the course of a few years, the level of the trenching ground sinks considerably and the whole area becomes a shallow depression where water stagnates during the rainy season, leading to general insanitary conditions. To avoid this, the municipalities do not sell the night-soil manure even though there is a demand for it. (2) In many towns, however,

there is no demand for it due to caste prejudice. The fields where trenching is done are sometimes leased out for cultivation and fetch a good revenue.

In the present efforts all over the country to increase the production of food crops, many are looking forward to fuller utilization of all wastes for agricultural purposes. The Provincial Governments are, therefore, operating compost schemes for converting town refuse into compost manure. In the preparation of compost from town wastes, both night-soil and *katchra* are together processed, and it is observed that the disposal is more sanitary than the older methods. The manure does not possess any offensive smell and hence it may be possible to make cultivators handle it themselves without any prejudice.

One criticism that is sometimes made by public health authorities regarding the compost method is that it does not prevent properly the breeding of flies. Our observations on the Bangalore method of composting have been quite satisfactory in this respect. In view of the above criticism, it was considered necessary to have some critical observations on fly breeding and these observations are reported here.

Experimental

Large-scale compost work was started at Amraoti in May 1944. Compost trenches of the size 20 × 6 × 3 feet were filled with refuse by the Bangalore method (1) by putting alternate layers of 6 inches *katchra* and 2 inches night-soil. The layer of *katchra* was made up by two cart loads and that of the night-soil by 100 gallons of fresh night-soil. The topmost layer of *katchra* in every trench was thicker (9 inches) being made up by three cart loads of rubbish, and this was finally covered over by a 2-inch layer of earth.

Temperature of compost mass during summer

The temperature of the top 9-inch layer of the compost mass was recorded in many trenches

TABLE I
Showing temperature of the top 9-inch compost mass for a period of a fortnight in trench no. 20

Day after complete filling of the trench	Temperature in centigrade
6	61°
7	61°
8	60.5°
9	65°
10	60°
11	62°
12	63°
13	62°
14	62°
15	64°
16	64°

* Abstract of the paper communicated to and published by the Agricultural Section of the 32nd Indian Science Congress. The work was conducted under the compost scheme financed partly by the Imperial Council of Agricultural Research.

from time to time by inserting a thermometer at three or four spots and noting the average temperature. It would be unnecessary to give all the temperature records here, the general feature of the records being the same. Some typical figures are mentioned in table I.

It was generally observed that during the summer months of April, May and a part of June, the top layer of rubbish attained a temperature above 55°C. within the first two or three days; the maximum temperature was attained within the first week, and this temperature was maintained for over a fortnight. The maximum temperature noted in some other trenches is given below :—

TABLE II

Showing maximum temperatures reached in some compost trenches

Trench number	Day after filling when the temperature was attained	Temperature in centigrade
9	4	61°
11	7	60°
13	4	61°
14	6	62°
16	8	61°
19	7	65°
20	9	65°
21	8	61°
22	6	62°
23	7	62°
24	6	60°
26	4	63°

It is thus seen that the top *katchra* layer, whereto maggots from the lower night-soil layers would creep for emergence, maintains a temperature condition which can be considered sufficient for their destruction. As the life-cycle of flies from the egg to the adult stage is 12 to 15 days, it is important that the highest temperature conditions develop and prevail within this period.

Maggot and pupal counts in the summer

The total number of maggots and pupæ present was counted in four or five in one square foot areas in some trenches. The *katchra* layer was disturbed to a depth of 3 inches or so, and

all maggots and pupæ carefully counted. The results are given below :—

TABLE III

Showing the number of maggots and pupæ per square foot in the surface rubbish layer in summer months

Trench number	Number of maggots	Number of pupæ
2	Nil	Nil
4	5	4
7	5	4
8	12	Nil
13	7	Nil
16	18	3
21	4	11
22	2	6
23	30	5
24	8	8
25	5	2
26	1	Nil

It is seen from the table III that the number of maggots and pupæ in the compost trenches is very low in the summer. It has been further observed that a large number of maggots were dead, probably because of the high temperature conditions prevailing in the compost mass. It may be concluded that the nuisance of fly breeding in the summer months does not exist, as a result of high temperature attained by the decaying rubbish which destroys a large number of fly maggots and pupæ, and also because the general conditions are also not very favourable to fly breeding during the time.

Temperature of compost mass during the rainy season

The rains particularly have been rather heavy this season at Amraoti. The total rainfall this year was 51 inches, whereas the average for this tract is only 30 inches. During the rainy season the general condition of moisture in the compost mass is unfavourable for rapid decomposition. Whereas the *katchra* during the summer is quite dry, and the proper moisture conditions for rapid decomposition could be established by the addition of the required quantity of night-soil, in the rainy season *katchra* is almost saturated with moisture, and hence the moisture level is much above the optimum. Excessive moisture prevails in the compost mass. This generally leads to slow decomposition and hence to a slight rise of temperature. The

maximum temperatures recorded in some trenches in the surface 9-inch layer of rubbish are given in table IV :—

TABLE IV

Showing maximum temperatures in centigrade recorded in some trenches in rainy season

Trench number	Day after filling when temperature was attained	Temperature in centigrade
46	4	54°
49	2	49°
52	9	38°
54	3	35°
60	15	43°
61	10	49°
62	4	50°

It is, however, observed that during the rainy season considerable variations occur in temperatures depending upon the rainfall conditions and consequently on the moisture and air conditions in the top compost mass in the trenches. The temperatures of the surface 9-inch layer of rubbish in trench no. 60 are given below as an example :—

TABLE V

Temperature in centigrade in the surface 9-inch layer of trench no. 60 during first two weeks

Day after filling	Temperature in centigrade
4	21.5°
5	35°
6	42°
7	37.5°
8	39°
9	40°
10	42°
12	49°
14	39°
15	43°
17	33°

It is thus seen that the temperature of the compost mass may vary considerably during the rainy season, low temperatures prevailing after heavy rain showers and higher temperatures when the weather clears up.

Maggot and pupal counts during the rainy season

The conditions in general in the rainy season are very conducive to fly breeding. The night-soil carts which arrive at the depot generally bring in their train an army of flies. The wet *katchra* also is highly infested with flies. It was not necessary to take a count of maggots and pupæ in the trenches which showed an overwhelmingly large number of them. During summer, *katchra* was generally free from fly maggots but during the rainy season a very large number of maggots occurred in the *katchra* also.

This is because of the fact that *katchra* is wet and contains a large proportion of cattle-dung (which in the dry season is converted into fuel cakes and sold) and also night-soil at some centres due to the habits of the local people. As a measure of fly infestation, the volume of *katchra* highly infested with maggots was recorded. The observations are given below :—

TABLE VI

Showing volume of katchra infested with maggots used for compost preparation in various trenches

Trench number	C.ft. of total <i>katchra</i> used for composting	C.ft. of <i>katchra</i> infested with maggots
53	360	210
54	360	240
55	360	180
56	360	120
58	360	240
59	360	180
60	360	210

It is thus seen that nearly one-third to half of the *katchra* used for compost preparation is infested with maggots. The fly nuisance, hence, is greater during the rainy season. It has been, however, observed that all the pupæ occurring in the compost trenches do not reach the fly stage even under favourable conditions. This was tested by collecting a certain number of pupæ from the trenches and breeding them in small fly cages. The results of these tests are given in table VII :—

TABLE VII

Showing the viability of pupæ from some trenches

Number of pupæ kept for breeding	Total number of flies emerged	Percentage viability
11 (trench no. 46)	2	18.1
60 (trench no. 50)	6	10.0
20 (trench no. 54)	4	20.0

It is seen from these data that the actual fly nuisance cannot be gauged from the number of maggots and pupæ occurring in the compost trenches. The viability of these appears to be about 10 to 20 per cent only. Further intensive tests may, however, be needed.

Summary and conclusions

Counts of maggots and pupæ, taken from time to time, in the top rubbish layer of compost trenches led to the following conclusions :—

1. During the months of April, May and June the number of fly maggots and pupæ in the surface rubbish layer of compost trenches is very low.

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2. The maximum temperature attained in the first week in the top rubbish layer ranges from 60°C. to 65°C. and is considered to be effectively lethal for maggots and pupæ present in the mass.

3. During the rainy season, a very large number of maggots and pupæ are observed in the trenches. The maximum temperature of the top rubbish layer in this season ranges from

37°C. to 49°C. These low temperatures and the humid atmospheric conditions probably promote fly breeding. Both night-soil and *catchra* are highly infested with fly maggots in this season.

4. The viability of pupæ occurring in compost trenches in the monsoon has been tested and it is observed that only 10 to 20 per cent of the pupæ can reach the fly stage when given favourable conditions.

Current Topics

Penicillin Therapy in Rat Bite Fever

By W. A. ALTEMEIER

H. SNYDER

and

G. HOWE

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXVII, 3rd February, 1945, p. 270)

1. THERE are at least two forms of rat bite fever, one caused by *Spirillum minus* and the other by *Streptobacillus moniliformis*.

2. The type caused by *Spirillum minus* responds well to arsenical therapy, but no satisfactory chemotherapeutic agent has been available for the type produced by *Streptobacillus moniliformis*.

3. A review of the literature reveals only 17 cases of rat bite fever due to *Streptobacillus moniliformis* in the United States in which the diagnosis was verified by recovery of the organism. Three more cases were treated for the first time with penicillin. The therapeutic response was prompt and permanent in the first 2 cases. In the third a relapse occurred after the administration of an inadequate amount of penicillin.

4. Studies *in vitro* indicated that penicillin has a powerful bacteriostatic effect on the three strains of *Streptobacillus moniliformis* recovered.

5. A comparison of the course of our cases with those previously reported gives the impression that penicillin is an effective chemotherapeutic agent which shortens decidedly the course of the disease.

6. In the future, treatment with penicillin is recommended in the therapy of rat bite and Haverhill fevers.

Treatment of Meningococcal Meningitis with Penicillin

(Abstracted from the *Medical Press and Circular*, Vol. CCXIII, 21st February, 1945, p. 114)

IN the present war the overall mortality from meningococcal meningitis in the Army and Navy is well under 5 per cent and there has been a remarkably low incidence of complications. These brilliant results have followed the use of the sulphonamides. There is, too, increasing evidence that anti-meningococcal serum may do more harm than good in drug treated cases. The sulphonamides have also been highly effective in the management of meningococcus carriers, particularly the mass elimination of such carriers from large military units.

Among the sulphonamide-treated cases of meningococcal meningitis there have been some failures, particularly in fulminating cases and in late and neglected ones. There have also been some failures owing to the improper use of the therapy which resulted in renal or other complications. There have, however, been few if any authentic cases in which

sulphonamide resistance of meningococci obtained from human cases was bacteriologically proved.

With the introduction of penicillin it was rational to explore its possibilities in this field. So far as it is now known, patients with meningitis require intrathecal as well as parenteral treatment with penicillin to control the meningeal infection. Intrathecal injection is accompanied by a definite inflammatory reaction and often by the signs and symptoms of meningeal irritation. These reactions are undesirable and often harmful, because they may interfere with prompt bacteriologic cure and may prolong and aggravate the clinical symptoms. The parenteral use of penicillin and even its use as a spray have apparently failed also to rid the nasopharynx of meningococci.

For practical purposes it may be said that sulphonamides still constitute the treatment of choice in meningococcal meningitis. From the information thus far available it seems wise to reserve penicillin for use as an adjunct to the sulphonamides in those patients to whom the drugs do not bring about an adequate clinical response or for use in patients to whom sulphonamides cannot be given. Penicillin may also prove helpful in the management of focal purulent meningococcal infections, particularly those of the joints.

Penicillin with Special Reference to Its Use in Infections Complicating Diabetes

By F. B. PECK

(From the *American Journal of Medical Sciences*, Vol. CCVIII, November 1944, p. 581, as abstracted in the *Journal of the American Medical Association*, Vol. CXXVII, 10th February, 1945, p. 356)

Penicillin in infections complicating diabetes.—Peck reports 15 cases of diabetes which illustrate that penicillin is remarkably efficacious in the infectious type of gangrene, osteomyelitis of the bones of the feet and the huge sloughing carbuncles. He never noted a deleterious effect on carbohydrate tolerance, nor has penicillin administration necessitated larger doses of insulin. The presence of infection notoriously increases the insulin requirement, but in none of the cases described was there any unusual difficulty.

The Treatment of Subacute Bacterial Endocarditis with Penicillin

By M. H. DAWSON, M.D.

and

T. H. HUNTER, M.D.

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXVII, 20th January, 1945, p. 129)

SUMMARY

TWENTY patients with subacute bacterial endocarditis were treated with penicillin. A preliminary group of

5 were treated in 1942 and 1943, and 15 were treated in 1944. The infecting organism was a streptococcus in all instances. Heparin was employed as an adjuvant to penicillin in the treatment of the majority. While it is recognized that a long follow-up will be necessary before the ultimate outcome is established, therapy was apparently successful in 15 of the 20. All 15 patients are now clinically and bacteriologically free from infection. In 2 of the remaining 5 patients the infection was controlled as long as penicillin was administered, but a relapse occurred when therapy was discontinued. These 2 patients are still in excellent general health, and it is hoped that it will yet be possible to arrange for a therapeutic regimen which will produce a satisfactory outcome. The remaining 3 patients succumbed. In each instance death was apparently due to a cerebral embolus. In 2 of the fatal cases the infection was still present at the time of death, and in the third the situation was in doubt. Further experience is necessary before an opinion can be expressed regarding the value of heparin as an adjuvant to penicillin in the treatment of this disease.

Effect of Rubber Tubing on Solutions of Penicillin

By S. T. COWAN, M.D., dipl. Bact. (Manch.)

MAJOR, R.A.M.C.

(Abstracted from the *Lancet*, i, 10th February, 1945, p. 178)

RUBBER was found to have a variable effect on penicillin solutions; some samples inactivated a considerable proportion of the antibiotic and others had no observable effect.

In continuous intramuscular infusion the long contact of solutions with the rubber tubing affords ample time for the destruction of 25 to 50 per cent of the penicillin if the rubber is unsuitable.

A simple method of testing the rubber is described.

Prolonging the Action of Penicillin

By M. J. ROMANSKY

and

G. E. RITTMAN

(From the *Bulletin, U.S. Army Medical Department*, October 1944, p. 43, as abstracted in the *United States of America Medical-Newsletter* No. 54, p. 8)

A COMPLETELY satisfactory method of administering penicillin has not yet been described. The high levels of penicillin in the blood resulting from the usual form of intramuscular injection lasts for only brief periods and for the treatment of most diseases frequent injections are required. Consequently, any method of administration which would prolong the duration of effective levels in the blood and would decrease the rate of absorption would be most helpful. In the effort to develop such a substance, Romansky and Rittman have reported a study in which beeswax-peanut oil was employed to decrease the rate of absorption of penicillin and to attempt to maintain a constant effective level in the blood over a longer period than is obtained by the use of the usual isotonic solution of sodium chloride. Preliminary investigations indicated that penicillin could be evenly distributed in a filtered beeswax-peanut oil mixture and that such a mixture is stable, showing no deterioration in various batches kept at refrigerator, room and 37°C. temperatures for 30 to 62 days. Early studies also indicated that effective levels of penicillin in the blood could be obtained by intramuscular injection of this mixture into rabbits and into human subjects. Clinical trial was then indicated: 12 patients with gonococcal urethritis were treated with single injection of penicillin in beeswax-peanut oil mixture; the doses varied between 51,250

and 100,000 Oxford units, which were contained in 2 to 3 c.c. of the mixture. Eleven of these patients (9 had been sulfonamide-resistant) were cured, as shown by freedom from clinical symptoms and negative smears and cultures two, five and seven days after treatment. Local pain or irritation in the region of the injection was not sustained by any of them, nor were there any undesirable constitutional reactions. This is the most promising report which has yet appeared on the development of an effective and delayed acting penicillin preparation.

The Therapeutic Indications of the Sulphonamides and Penicillin

By F. G. BLAKE

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXVII, 3rd March, 1945, p. 517)

THE infections which are curable or, if not cured, favourably modified by the chemotherapeutic agents under discussion may be divided into three groups with respect to aetiology:

1. Those in which both the sulphonamides and penicillin are more or less effective, though not necessarily equally so, namely certain Gram-positive and Gram-negative coccic infections: hæmolytic streptococcus, pneumococcus, staphylococcus, *Streptococcus viridans*, meningococcus and gonococcus.

2. Those in which the sulphonamides are of value but not penicillin, namely Gram-negative bacillary infections such as those caused by the colon bacillus, dysentery bacilli, *Hæmophilus influenzae*, Friedländer's bacillus and Ducey's bacillus.

3. Those in which penicillin is of value but not the sulphonamides, namely syphilis, yaws and possibly other spirochætal infections and those due to the *Clostridia*—gas gangrene.

As for the first group, in the less severe hæmolytic streptococcal infections in which there is tissue invasion without suppuration, necrosis or bacteraemia, such as erysipelas or lymphangitis, the sulphonamides are ordinarily sufficiently effective to be indicated as the drug of choice, if for no other reason than because of simplicity of administration. The same may be said of the milder upper respiratory mucous membrane infections, such as tonsillitis or pharyngitis, although the real value of the sulphonamides in these infections is still debatable.

In the more severe hæmolytic streptococcal infections with suppuration or necrosis and with or without bacteraemia penicillin appears to be much more effective and consequently the drug of choice. It often succeeds in bringing about a cure when the sulphonamides have failed. Included in this group are severe cellulitis, mastoiditis with or without intracranial complications, meningitis, pneumonia, empyema, pericarditis, endocarditis, peritonitis, puerperal sepsis, osteomyelitis, suppurative arthritis and infected wounds. In such conditions as empyema, meningitis and arthritis it must be injected locally as well as intravenously or intramuscularly.

In pneumococcal infections the sulphonamides have proved sufficiently effective in lobar pneumonia to justify their continued use as the drug of choice at the beginning of treatment, but one should be prepared to shift to or add penicillin promptly in cases that do not respond quickly to the sulphonamides. In very severe pneumonia and particularly in the aged and in other pneumococcal infections such as mastoiditis, meningitis, empyema, endocarditis and peritonitis penicillin is more effective and consequently indicated from the start.

In staphylococcal infections such as furunculosis, carbuncles, osteomyelitis, mastoiditis with or without intracranial complications, meningitis, sinus thrombosis, pneumonia, lung abscess, empyema, pyelonephritis and wound infections with or without staphylococemia the sulphonamides, though occasionally beneficial, have or

the whole been disappointing. Penicillin, on the other hand, has proved very effective in a high proportion of cases and is unequivocally the drug of choice. Failures do occur, of course, possibly because of the fact that some strains of staphylococci contain penicillin inhibitor, as recently shown by Kirby, similar in its inhibiting action to the penicillinase found in colon bacilli.

Streptococcus viridans subacute bacterial endocarditis has rarely responded more than temporarily if at all to the sulphonamides. Recent experience with large amounts of penicillin given in three to four-week courses indicates that in some cases it may be effective in inducing remissions. Although much more experience is needed to define its ultimate usefulness, its trial at least is indicated.

In the two important Gram-negative coccic infections, meningococcal and gonococcal, the sulphonamides have proved so effective in the former that they are still indicated and penicillin should be resorted to only in those cases which fail to respond to the sulphonamides or possibly as an additive treatment in the very severe fulminant cases.

Penicillin, now demonstrated to be more effective than the sulphonamides in curing gonococcal infections, would appear to be indicated at least in all cases complicated by arthritis, ophthalmia, endocarditis, pericarditis, peritonitis, epididymitis and prostatitis and in all cases of sulphonamide resistant gonorrhoea. Whether it will properly replace the sulphonamides in simple acute urethritis remains to be determined.

Of the second group of infections, in which the sulphonamides are indicated and penicillin is contra-indicated because it is ineffective, little need be said except to reiterate that they comprise a group of Gram-negative bacillary infections including colon bacillus infections, particularly of the urinary tract, *Hæmophilus influenzae*, otitis media, mastoiditis and meningitis, the bacillary dysenteries, Friedländer bacillus infections, including pneumonia and soft chancre.

Similarly little need be said of the third group, in which the sulphonamides are of little or no value and in which penicillin appears to be indicated, other than to state that the exact usefulness of penicillin in human clostridial infections remains to be determined and the final definition of its already established usefulness in syphilis will require prolonged study.

The Effect of Para-Aminohippuric Acid on Plasma Concentration of Penicillin in Man

By K. H. BEYER

and
OTHERS

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXVI, 16th December, 1944, p. 1007)

In human beings, as in dogs, one can either effect a considerable economy of penicillin or maintain plasma concentrations of the antibiotic agent not heretofore practicable when penicillin together with sodium para-aminohippurate is administered continuously by venoclysis. Very few secondary effects have been observed to attend the combined use of these compounds in this study.

New Drug in Typhus

(From the *Medical Press and Circular*, Vol. CCXIII, 14th February, 1945, p. 99)

THE U.S.A. Typhus Commission Unit at the Fever Hospital in Cairo report that para-aminobenzoic acid seems to exert a definitely beneficial effect on the course of louse-borne typhus. Among seventeen patients between the ages of eighteen and forty-eight who were given the drug during the first week of illness there were no deaths, whereas among forty-four

untreated cases in the same age group, eight deaths occurred. Among two supplementary cases who were given the drug after the first week of illness one died. Another, a man over seventy, also died in spite of treatment beginning at the third day of illness. This seems to be one of the few remedies of promise in the treatment of epidemic typhus one of the great plagues of mankind. The study on which the report is based was made possible through the courtesy of the Egyptian officials who allowed the Typhus Commission to establish an experimental ward in the Cairo Fever Hospital early in 1943, just at the beginning of one of the most severe epidemics of typhus which Egypt has experienced. None of the patients had been vaccinated against typhus. The initial dose of para-aminobenzoic acid varied from four to eight grammes, given by mouth and followed up by two-gramme doses every two hours until the concentration in the blood became excessively high. The two-hourly routine was adopted because of the rapidity with which the drug is excreted. Nausea and vomiting attributed to the drug occurred among the first few patients, but thereafter was largely controlled by giving sodium bicarbonate in addition. The optimum dosage is, however, yet a matter to be settled. All that can be said so far is that para-aminobenzoic acid seems to have a beneficial effect on typhus, but the reason for this is not clear. It is quite possible that it may exert an equally beneficial effect in other rickettsial diseases.

Louse-Borne Typhus Fever: Trial of Serum Treatment

By R. S. STEVENS

(Abstracted from the *Lancet*, i, 27th January, 1945, p. 106)

TWENTY-ONE cases of louse-borne typhus fever were treated at a military hospital in the Middle East in 1943.

Antityphus serum (Lederle), supplied by the U.S. Army medical services for clinical trial, was used in seven cases.

Six cases were given large doses of serum as soon as clinical diagnosis was established and all recovered. A seventh case, given a smaller dose, died.

No attempt is made to draw conclusions from so small a series, but reasons are given for believing that the serum has a beneficial effect by modifying the severity of the course and reducing the toxæmia.

Emphasis is placed on giving the serum as early as possible and in adequate dosage.

Two School Outbreaks of Streptococcal Throat Infection

The Effect of Sulphonamide Lozenges on Carriers

By R. L. VOLLUM, M.D., D.Phil.

and

G. S. WILSON, M.D., F.R.C.P., D.P.H., K.H.P.

(Abstracted from the *British Medical Journal*, i, 21st April, 1945, p. 545)

FROM the limited observations recorded it seems clear that a prophylactic dose of 6 gr. daily of mixed sulphapyridine and sulphathiazole given in the form of lozenges is unable to protect children from streptococcal infection; and that neither 6 nor 12 gr. daily for 5 to 7 days is able to clear streptococci from the throats of healthy or convalescent carriers. Hayden and Bigger also found that the incidence of respiratory disease in an Army unit was apparently unaffected by the prophylactic administration of 5 lozenges a day for 16 days, each lozenge containing 1 gr. of sulphanilamide; and Wright showed that sulphanilamide or

sulphathiazole in large doses—46 to 116 gr. daily—was unable to prevent streptococcal cross-infection of children in measles wards. They are, however, at variance with American observations. For example, Watson Schwentker, Fetherston, and Rothbard describe how an epidemic of scarlet fever due to type 19 in a naval station was rapidly brought under control by a dose of 1 g. (15 gr.) of sulphadiazine a day, given either in a single dose or in two divided doses. Though it is not disputed that cases ceased to occur about a month after starting the treatment, examination of the carrier rates provides very little evidence that sulphadiazine had any important effect, either prophylactically or therapeutically, on the frequency of infection.

More recently Holbrook in the Army and Coburn in the Navy have described the effect of mass prophylaxis with sulphadiazine, and claim to have achieved a reduction of 50 to 85 per cent in the incidence of streptococcal infections of the respiratory tract by administration of 1/2 to 1 g. (7 to 15 gr.) of this substance daily. No figures on carrier rates are given, but Coburn states that a continuous daily dose of 1/2 g. was sufficient to prevent 85 per cent of the exposed population from becoming infected with hæmolytic streptococci.

What is the cause of the discrepancy between the British and the American experience? It may be objected that our observations were on far too small a scale to admit of any reliable deductions being made from the results. Though not denying that our test population was numerically insignificant compared with that of Holbrook or of Coburn, we would point out that our observations were made in residential schools, where the exposure to risk was relatively uniform, and that they were carefully controlled bacteriologically. Under such conditions, we believe that the complete failure of sulphonamides, in a dosage similar to that used by the American workers, to exercise any prophylactic or therapeutic effect cannot be dismissed as unimportant on statistical grounds. The method used by Holbrook and by Coburn and also by Garson, who reported good results from the prophylactic administration of 4 gr. of sulphanilamide a day in lozenge form—was to treat some units in the Army and the Navy, leaving other units to serve as controls. The wisdom of this procedure seems to us to be questionable. It is impossible at present to foretell how streptococcal infection will develop in any segregated or institutional population, even when the distribution of infection has been carefully mapped out by bacteriological means beforehand. Experience of several outbreaks investigated by the Oxford laboratory has shown that a low carrier rate may be followed by numerous cases, and a high carrier rate by few. Similar observations have been made by Hamburger in the spread of streptococcal infection in American army hospital wards. It is therefore hazardous to draw conclusions from the behaviour of an infection in different units. Instead of treating all men in alternate units, it would be more satisfactory to treat alternate men in the same units.

Our conclusion, therefore, is that a case has not yet been made out for mass prophylactic treatment of populations exposed to streptococcal infection.

The Use and Abuse of Nasal Vasoconstrictor Medications

By B. M. KULLY

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXVII, 10th February, 1945, p. 307)

No class of drugs is more widely distributed and used than are nasal vasoconstrictors. This is due to advertising of 'patent' nostrums in press and radio, to exploitation of new compounds to the profession by pharmaceutical houses and to wide prescription of these drugs by physicians. Tabulation reveals that there are nationally distributed at least 240 nasal vaso-

constrictor compounds in the form of drops, sprays, inhalants and ointments. It is timely to question whether the increased use of vasoconstrictors is justifiable and whether there are not disadvantages inherent in these drugs which demand a reappraisal of the indications for their use.

The action of sympathomimetic drugs on the nasal mucosa is directed chiefly to the blood vessels, though the secretory function also is affected. Primarily the effect on the blood vessels is vasoconstriction. The subepithelial capillaries and arterioles as well as the venous sinuses of the erectile tissues are constricted. Nasal secretion is diminished in contrast to the increased secretion that occurs when vasoconstriction results from chilling of the body surfaces.

Sympathomimetic drugs vary in the intensity and the duration of the primary constricting effect and in the severity of their secondary dilating effect. Epinephrine and amphetamine are examples of drugs causing severe reactions, ephedrine and neosynephrin represent those producing a milder reaction. The amount of secondary congestion is proportionate to the intensity of the vasoconstriction, the frequency with which the drug is employed and the period of its use.

In recent years there has been a tendency to incorporate antiseptics with vasoconstrictors. This is particularly true of the sulfonamides, which have been added to almost every type of vasoconstrictor. The rationale of the use of antiseptics is questionable. They are in contact with limited areas of the nasal mucosa and then for brief periods of five to fifteen minutes. As shown by Walsh and Cannon, they do not penetrate into the subepithelial tissues where the infecting organisms thrive. They increase irritation and reaction.

The use of vasoconstrictors in the form of inhalants has become popular in recent years. Of these, amphetamine evokes the most vicious reaction because of its powerful pressor action and the ease of self-administration. Reactions equally severe are caused by some of the 'patent' inhalers.

In nasal surgery, vasoconstrictor medication is a requisite. Bleeding is controlled, the field of vision widened and absorption of the anæsthetic delayed. The use of a drastic vasoconstrictor, epinephrine, is justified, though post-operative swelling may be due more to the drug than to the surgery. Vasoconstriction is necessary in many manipulative procedures, such as sinus irrigations. In the displacement method of Proetz it is invaluable for therapy or visualization. Yet there has been observed damaging after-congestion with involvement of previously uninvolved sinuses, following too frequent displacement treatment or the use of drastic medication.

The value of vasoconstrictor therapy for acute rhinitis is questionable. The distress of the patient is temporarily relieved, justifying, in some instances, careful and minimal use of a mild decongestive drug. Unfortunately, such care is rarely exercised and the result is a disturbance in the nasal defence mechanism.

It is not implied that nasal vasoconstrictors are contra-indicated in the treatment of acute sinusitis. To shrink carefully the swollen mucosa about the orifice of an acutely infected sinus is a rational procedure. However, the margin between therapeutic shrinking and that of after-dilatation worse than the original condition is not a wide one and demands conservative judgment.

Streptothricin

(From the *Medical Press and Circular*, Vol. CCXIII, 7th February, 1945, p. 83)

THE chemotherapeutic agents introduced within recent years have been mainly effective against Gram-positive bacteria, but since 1940 investigations into antibiotics effective against Gram-negative organisms have shown that streptothricin, obtained under certain

conditions from 'Actinomycetes Lavendulæ', is highly active against all Gram-negative bacteria tested. Pure strains of mice were used for the *in vivo* studies, and pathogenic highly mouse-virulent cocci and bacilli were employed in the tests. Activity against influenza virus and a strain of trypanosoma equiperdum was also investigated.

The toxicity of the streptothricin on the test animals and the relative effectiveness against a wide variety of organisms are tabulated. It was found that organisms of the 'colon-typhoid', and 'salmonella' groups were particularly affected by the crude streptothricin, but 'B. pyocyaneus' and 'B. proteus' were more resistant. Activity of the drug was reduced, but not completely destroyed, by oral administration, and it is noted that strong acids have little effect on streptothricin, unlike penicillin. It appears that bacillary dysentery, typhoid fever and food poisoning by the 'salmonella' group might be expected to respond to streptothricin administration.

The final evaluation however, it is pointed out, will depend on the nature of the toxic effects produced by various dosage regimes. These have yet to be completely investigated.

The Value of the Sedimentation Test in Pulmonary Tuberculosis

By G. I. DAVIES

(Abstracted from the *Medical Press and Circular*, Vol. CCXIII, 21st March, 1945, p. 186)

It is in pulmonary tuberculosis, however, that the test has found its highest application and value, but whilst no diagnostic specificity is claimed for it, there is universal agreement that its prognostic value is a very real one and that it is also an excellent therapeutic index.

Prognosis in pulmonary tuberculosis is very uncertain, does not conform to any orthodox sequence of clinical features, and even a lifetime of experience does not always carry with it the conviction of accuracy, since the physical signs bear no substantial relationship to the functional efficiency of the lungs.

Briefly summarized the test depends upon the fact that in certain physiological and pathological conditions the erythrocytes in a column of citrated blood gravitate to the lower end of a vertical tube more rapidly than under normal conditions.

Avoid carrying out the test when the following associations are present:—

- (1) Anæmia.
- (2) Menstruation.
- (3) Pregnancy.

The results obtained under such conditions are not strictly accurate.

Normal values of the rates of fall will be found between 0—10 divisions.

CLASSIFICATIONS OF RATES OF FALL

For simplicity the following classifications might be adopted as a prognostic guide.

1. Type A, 0-10.—This is given by normal persons and doubtful cases of pulmonary tuberculosis. In cases of proved tuberculosis it indicates well-established resistance—quiescent and arrested disease—prognosis excellent.

2. Type B, 10-20.—This is given by patients whose resistance is in the balance, and the turning of the scales in the direction of A or C curves is determined by early and suitable treatment on the one hand, or neglect and increased activity on the other hand. Patients with this type are very suitable for sanatorium treatment and the prognosis is usually very good.

3. Type C, 20-40.—This is more advanced than B and, in order to produce improvement, specialized therapy in sanatorium or chest hospital is usually necessary. Prognosis can be judged by monthly sedimentation records.

4. Type D, 40-60 and over.—This is given by rapid, advanced and complicated cases, where activity is well marked and signs and symptoms pronounced and troublesome. Prolonged rest is essential—reaction to treatment is slow and the prognosis invariably poor. The greater the fall beyond 60, the worse is the prognosis in untreated cases.

SOME CONDITIONS AFFECTING THE B.S.R.

1. *Pyrexia*.—It is found that, irrespective of the causative factor, pyrexia always causes an increased B.S.R., and the severity of the pyrexia is proportional to the increase.

2. *Complications*.—Increased B.S.R. can and will occur a few hours or even days before the obvious warning of clinical signs of complications. Routine tests will often demonstrate the truth of this statement.

3. *Pregnancy*.—Pregnancy associated with pulmonary tuberculosis has a definite effect upon the B.S.R. in the nature of increasing the rate gradually with the advancement of the pregnancy, and irrespective of any effect which this physiological condition has upon the pulmonary lesion.

4. *Hæmoptysis*.—The collective evidence and general summary in such cases point to the fact that hæmoptysis of pulmonary origin indicative of activity is associated with an increased B.S.R., whereas in hæmoptysis of extra pulmonary origin and of a mild degree, no such increase is discovered.

5. *Treatment*.—Sedimentation graphs during treatment, either symptomatic in nature or by specialized therapy, including thoracic surgery, depict the clinical course and response to treatment. Improvement in the clinical picture is followed by a diminished B.S.R., a stationary course by a stationary graph, whilst exacerbations and complications are represented by an increased rate. It can therefore be said that any form of therapy which does not produce an improvement in the B.S.R. should be regarded as valueless and immediately abandoned.

Dextran as a Substitute for Plasma

(From the *Lancet*, i, 3rd February, 1945, p. 152)

FURTHER information has now appeared concerning dextran, which has been claimed to be an efficient substitute for blood plasma in transfusion. The substance is a neutral polysaccharide, consisting of a water-soluble high-molecular carbohydrate formed in solutions of sugar by the bacterium *Leuconostoc mesenteroides*. Its molecular weight may be many millions, but by partial hydrolysis preparations with molecular weights of 100,000 to 200,000 can be made, though these like the original are not homogeneous with respect to molecular weight. It is claimed that a solute can be prepared by partial hydrolysis which does not give rise to reactions or undesirable sequelæ even after repeated large infusions. The viscosity and colloidal osmotic pressure of the 6 per cent solutions (with 1 to 3 per cent sodium chloride) which were used for experimental work were about the same as those of blood. After a single intravenous dose the dextran concentration in the blood of a dog falls gradually to zero in three or four days during which time dextran of lower molecular weight than the original injection can be detected in the urine. There is no evidence of storage, even after repeated large infusions—an advantage over the otherwise efficient gum-saline solutions. Infusions are said to have rapid and lasting effects on the blood pressure, heart action, and respirations of rabbits and cats subjected to bleeding, histamine shock, and confusion shock, while preliminary clinical trials have suggested that dextran is a better plasma substitute than gum-arabic, polyvinylpyrrolidone ('Periston'), or pectin. Dextran increases the sedimentation rate in the same way as gum-arabic, and this makes determination of the blood group a difficult matter.

An easily prepared and efficient plasma substitute would greatly relieve the strain on the blood-donor panel, and such a substance would not carry the ever-present menace of transmissible disease, due to a virus which not even filtration methods can remove. The assessment of dextran's claims, however, will need to be thorough and probably protracted before it can be said with confidence how far this carbohydrate is a complete substitute for natural blood proteins.

Pregnancy Tests

(From the *Lancet*, i, 6th January, 1945, p. 23)

THERE are now three tests for pregnancy which depend on the demonstration of an increased quantity of chorionic gonadotrophin in the urine. It is hard to know what names to use for them. Reference to the animal employed may lead to confusion—the 'mouse' test sounds all right, but the 'rabbit' test is often misheard as the 'rapid' test, and as for the third, the animal is strictly speaking neither frog nor toad, and 'xenopus' sounds rather pompous. The use of eponyms is the commoner practice, though the names Aschheim, Friedman, and Hogben are frequently misspelt.

The Aschheim-Zondek test has already proved its reliability, and for many years Professor Crew was able to report a very low percentage of error with it from the Edinburgh Pregnancy Diagnosis Station. Almost every step in the procedure, from the preliminary weighing of the mice to the diurnal injections, the gassing and the dissection and mounting of the ovaries, can be left to the trained technician, and only the inspection and reading of the ovaries need be undertaken by the director of the station. A big colony of mice, or a reliable supplier, is essential. By using 5 mice for each test, the occasional refractory animal is virtually eliminated, and false positives should be rare provided the weight and therefore the age of the mice has been carefully checked. The great disadvantage of this test is that it takes 5 days to perform.

The Friedman test, which is now almost as well known, is perhaps more suited to the smaller laboratory than to the pregnancy diagnosis station. Small numbers of doe rabbits need to be kept in stock and each strictly segregated not only from bucks but from other does. The intravenous injection of the untreated, or simply filtered, urine demands some technical skill which is acquired by practice. Results may be read in 48 hours. The test animal can be eliminated as a possible source of error. A preliminary laparotomy will allow inspection of the ovaries before the test is begun; 48 hours after injection of the urine for diagnosis another laparotomy may reveal the characteristic corpora lutea and hæmorrhagia of a positive test, or it may reveal no change in the appearance of the ovaries. Injection of a known urine of pregnancy will now make sure that the individual rabbit will respond to chorionic gonadotrophin, and that the appearances found after the second laparotomy, were those of a true negative test. This procedure, while bestowing on the test a high degree of accuracy, renders it unsuitable for use on a large scale.

The Hogben test has the great advantage of speed, and only those familiar with pregnancy diagnosis tests will appreciate how important that is. A woman, content to have missed her period by many days, will suddenly decide that she must know at once whether she is pregnant or not. Xenopus will give her the answer within a day. For some years difficulty was experienced in this country with the Hogben test because it was impossible to breed the animals. This difficulty has now been overcome. There is nevertheless one serious disadvantage to the test—if untreated urine or alcohol-precipitated extract is injected, it kills 15 per cent or more of the animals. Preparation of the urine to make it less lethal is an elaborate process depending on the adsorption of the gonadotrophin on

kaolin, but in a pregnancy diagnosis station this can of course be carried out on a large scale without seriously inconveniencing the organization. It is advisable to kill animals not showing extrusion of ova overnight, for in some cases ova are found in the oviducts on post-mortem examination and an apparently negative test may prove to be positive.

From each of these three standard tests an accuracy of about 98.5 per cent may be obtained provided a detailed technique is developed in the hands of experienced workers. The Friedman test is suited to the small laboratory with a qualified research worker who will conduct most of the steps of the tests himself. The Aschheim-Zondek and Hogben tests are more suited to the pregnancy diagnosis station where such manipulations as multiple injections of animals and chemical preparation of the urine can be placed in the hands of trained technicians, the reading of results being alone left to a qualified director. Under such conditions minor variations in technique assume less importance.

Sterility : An Audit of 407 Cases

By ALAN GRANT

(Abstracted from *The Medical Journal of Australia*, Vol. I, 10th February, 1945, p. 134)

THE INVESTIGATION OF STERILITY IN THE MALE

THE minimum facts that should be known about a specimen of seminal fluid are as follows:—

The first is the volume. The second is the total spermatozoa count. It is essential to know the minimum number of spermatozoa present per cubic centimetre. This is estimated with the aid of a hæmacytometre chamber after dilution with 'Chloramine T'. The third essential is a differential sperm count. This means the estimation of the percentage of sperms present that have morphological abnormalities of their heads or tails. It is found by making a thin smear and fixing it with methyl alcohol and then staining it in a special manner.

The hydrogen ion concentration can be disregarded. The time has passed when it was sufficient to collect a specimen, look at it under a microscope, and pronounce a verdict as to the fertility of the donor, because motility is not synonymous with fertility, and abnormal spermatozoa can be quite motile.

THE CRITERIA OF NORMALITY

The following are the minimum requirements for normality:—

A volume below one cubic centimetre is abnormal. A total count of less than 50,000,000 spermatozoa per cubic centimetre is unsatisfactory and subnormal, providing that other abnormalities also are present. If over 20 per cent of the spermatozoa are of abnormal forms, the specimen is subnormal. An increasing percentage of abnormal sperms is progressively bad. In a normal sample about 70 per cent to 80 per cent of the spermatozoa should be motile if the specimen has been collected and transported properly. If there is no motility, be wary of jumping to conclusions, and repeat the test while looking for associated morphological deformities.

DEFICIENT SPERM COUNTS

Absence of spermatozoa calls for a testicular biopsy to see if spermatogenesis is normal. If it is, we may assume that there is a block in the ejaculatory mechanism. In the case of patients who have sperms in the specimen, but whose sperm counts are abnormal, the cause will usually be found to be constitutional and not local. Often a defective count is associated with excessive sedentary work, focal sepsis *et cetera*. If no organic disorder is discovered, the patient should be sent for a holiday in the open air, as this is more

enjoyable than a course of hormone therapy and much less expensive, and in our cases it proved effective.

THE RESULTS OF INVESTIGATION IN THE MALE

In our series of cases it was found that a little over 10 per cent of the males examined had no sperms in their ejaculate, or else had a negligible number. The quantity of seminal fluid that these men bring for examination is often large, all composed of secretions. The incidence of males who had subnormal sperm counts varied from 10 per cent to 15 per cent, according to the group of 100 cases on which the figures were based.

The lesson is that in any group of married couples suffering from childlessness, there is probably one family in every five in which the fault will be found on the male side. With regard to the treatment of males whose ejaculate contains sperms, but in unsatisfactory numbers, I should like again to stress the fact that holidays are to be tried before hormones.

INVESTIGATION AND TREATMENT OF STERILITY IN THE FEMALE

Most of these patients were investigated with lipiodol, 'Neo-Hydriol' (a less viscous oil) or 'Perabrodil' diluted with gum-acacia. The last-mentioned medium overcomes the fear that oil may be injected into the uterine veins. It is the opinion of the staff at the hospital that this danger has been overstressed in the literature. It is probably wisest to use gas first, and then to resort to some opaque medium if there is not an easy flow of gas at low pressure through the tubes. 'Oil often passes when gas will not.' The best time for these tests is the midmenstrual interval, when the mucosa of the tubes and uterus is not swollen and oedematous as it is in the premenstrual phase.

PREMENSTRUAL BIOPSY

The taking of a biopsy specimen may be carried out with safety in the surgery or out-patient department under local anaesthesia. The endometrial tissue should be removed from the anterior or posterior wall of the uterus high up, as it is there that the maximal cytological changes will be found. These fragments may be removed in the first four hours of the menstrual flow in the case of patients who have an irregular onset of the menses. A description of the changes to be looked for may be found in any standard textbook.

From the microscopic appearance of the endometrium it is possible to say whether the patient has ovulated or not. The patient who suffers from an ovulation has a discharge *per vaginam* each month like her normal sisters, but usually the menses are irregular in onset. Regular menstruation usually means ovular menstruation. The examination of endometrial biopsies is therefore urgent if a patient suffering from sterility is not menstruating at regular intervals. Apparently 'attacks' of an ovulatory menstruation are not uncommon in the human female.

THE TREATMENT OF BLOCKED FALLOPIAN TUBES

The surgical treatment of Fallopian tubes blocked at their fimbriated ends has not yielded more than about one pregnancy for every fifteen operations, and of these about one-third will end in miscarriage or ectopic gestations (Greenhill).

I think that more extensive use should be made of repeated insufflations or oil injections, either alone or with the additional therapy advocated by Moore-White of the Royal Free Hospital, London. In this regime five milligrammes of oestradiol benzoate are injected every five days for five injections, and the Fallopian tubes are then reinjected with an opaque medium. In a small series of forty patients treated by this method one-third had some degree of potency after the treatment, and about half of them are known to have become pregnant.

THE TREATMENT OF AN OVULATION

There appear to be two types of an ovulation, one of which is permanent and the other transitory. In

assessing the value of apparently successful treatment, one must always be suspicious that he is dealing with a case in which spontaneous cure not due to the medication provided has occurred. The only preparation for which any success at all can be claimed is serum gonadotropic hormone. I have used this subcutaneously and intravenously, but with doubtful success. Those patients who did commence to ovulate may have done so with the natural effusion of time.

THE TREATMENT OF OTHER INFERTILITY FACTORS

Genital hypoplasia is common, and may be treated by curettage, which seems to have a stimulating effect in promoting growth: or the oestrogenic hormones may be tried. The exigencies of army life make it impossible for me to have access to my statistical records on hypoplasia until some future (post-war) date.

Chronic cervicitis is common in sterile patients, and its treatment by linear cauterization yields highly satisfactory results. The unexplained feature about this lesion is that one finds it present in many successful *multiparae* who are not harassed by sterility.

The general health of the patient is of the utmost importance and diseases such as anaemia, vitamin deficiency conditions and subglandular states should be treated. The rôle of vitamin E is still undetermined, but it is certainly not a panacea that cures sterility without the trouble of physical examinations, sperm counts and tubal potency tests.

The most useful single glandular preparation is thyroid extract, and if it is used empirically it will serve the clinician well. The reason for this effectiveness of thyroid extract is unknown.

The Use of the Dried Blood Agglutination Test in the Diagnosis of Typhoid Fever

By W. GOETERS

(Abstracted in the *Bulletin of Hygiene*, Vol. XIX, September 1944, p. 678, from *Ztschr. f. Immunitats f. u. Exper. Therap.*, Vol. CIV, 30th December, 1943, p. 437)

THE agglutination test with dried blood, which is already used in the diagnosis of typhus, may be used as an aid to the rapid diagnosis of typhoid fever. Three separate drops of blood made with a 2 mm. loop are spread over an area 1 cm. in diameter on a slide and dried in the air. For the test the three drops are mixed respectively with 0.02 c.c., 0.04 c.c. and 0.08 c.c. of a formol-saline suspension of *Bact. typhosum* sensitive to H and O agglutinins. The drops are observed in a moist chamber at times up to 15 minutes.

Agglutination in the second and third drops was found to correspond to tube agglutination to a titre of 1/100 and 1/200, and is considered to be of diagnostic significance in uninoculated persons with no previous history of enteric fever. A positive result in the first drop only is regarded as a weak reaction demanding further investigation.

The dried blood test was found of value in the rapid differentiation of typhoid and typhus fevers.

Tetanus

By LESLIE COLE

(Abstracted from the *British Medical Journal*, i, 17th February, 1945, p. 219)

AFTER describing two cases of tetanus, the author makes the following comments:—

Local tetanus occurs in mild cases most commonly after prophylactic antitoxin has been given. Usually the local signs occur in the injured limb before any generalized symptoms appear. In head wounds, paralysis or spasm of cranial nerves, particularly the 7th and sometimes the 3rd, 6th and 9th, is another manifestation of local tetanus. It is an important

warning that generalized tetanus will almost certainly develop and an indication for giving antitoxin with the utmost dispatch without waiting for trismus or other generalized signs to appear. The work of Abel *et al.* suggests that local tetanus is caused by toxin absorbed from the wound affecting the motor nerve endings locally before toxin carried round in the blood stream has had time to produce its effect on the motor nerves generally or to involve the synapses in the brain and spinal cord.

In case I the signs of local tetanus in the wounded limb were very slight when the signs of generalized tetanus were marked, and it was only after antitoxin had been given that the local tetanus developed to an intense degree, persisting throughout the whole illness and even longer than the signs of tetanus in other parts of the body. It is perhaps worth noting that local tetanus of the type described in this case probably occurs without any detectable signs or symptoms of generalized tetanus later.

Case II is an example of severe tetanus with a period of onset of not more than 36 hours. The whole march of the disease in its early stages suggested a very bad prognosis. The case is described to illustrate the use of three measures which proved particularly helpful in treatment, namely, (1) intramuscular paraldehyde to control reflex convulsions and promote sleep; (2) a plaster-of-paris bandage to keep the needle of the intravenous drip in the vein during the period when convulsions were frequent and severe; (3) the early administration of sulphathiazole when the possibility of lung infection was threatening.

Reviews

MEDICAL BACTERIOLOGY: DESCRIPTIVE AND APPLIED INCLUDING ELEMENTARY PROTO-ZOOLOGY AND HELMINTHOLOGY.—By L. E. H. Whitby, C.V.O., M.A., M.D. (Camb.), F.R.C.P. (Lond.), D.P.H. Fourth Edition. 1944. J. and A. Churchill Limited, London. Pp. ix plus 342, with 81 illustrations. Price, 14s.

In revising this small work for a new edition, an effort has been made to preserve its original character, *viz.*, description of elementary and essential bacteriological facts and their application to practical medicine. There is a new chapter on chemotherapy, while the sections on gas gangrene, viruses and water analysis, and a few others have been brought up to date in the light of recent work and war experience.

HAIR AND THE SCALP.—By Agnes Savill, M.A., M.D. (Glas.), F.R.C.P.I. Third Edition. 1944. Edward Arnold and Co., London. Pp. xi plus 304. Illustrated. Price, 16s.

Most people are so concerned with the preservation and appearance of their hair that in case of troubles they first turn to advertisement rather than to doctors. It must be admitted that the general practitioners' knowledge of diseases of the hair and scalp is often limited to the use of a few ointments and lotions, and he is apt to regard them as of comparatively little importance; yet to the sufferer, women in particular, they seem far from trivial. Dr. Savill's book supplies a gap in our knowledge on the subject. So many additions and alterations have been made in this edition that it is practically a new book. She gives much information about the normal care of the hair and the effects of such procedures as permanent waving, singeing, bleaching and dying of hair. Falling hair from various causes occupies a good part of the book. All common disorders of the scalp and hair have been dealt with and emphasis is placed on their relation to internal diseases. The last chapter is on hirsutes. The book is practical and deserves a place on the doctor's shelf.

INTRAVENOUS THERAPY.—By K. V. Thakkar, L.M. & S. Second Edition. 1944. Published by K. V. Thakkar, Medical Building, Mama, Kotha Road, Bhavnagar, Kathiawar. Pp. xvi plus 350, with a coloured frontispiece and 10 illustrations. Price, Rs. 8-8

In this edition, the author has added a long list of medicines for intravenous therapy and omitted some, but we wish the omissions were a little more liberal and had included, to give a few examples, carbon in acute infections, acriflavin in gonorrhoea, colloid copper in phthisis and septicæmia, sodium fluoride for Graves' disease, perchloride of mercury in acute bacterial infections, etc. Otherwise the revision has been done with care and fairness to the different views held on the uses of the drugs. We doubt whether the author has been wise to include in the book several pages of advertisements of patent medicines, mostly of injectable nature.

ESSENTIALS OF DERMATOLOGY.—By Norman Tobias. Second Edition. Publishers: J. B. Lippincott Company, London. Price, 28s. net

The book covers practically the whole subject of dermatology and gives more details of symptoms, diagnosis and treatment than are commonly given in books of the synopsis type. The information given is up to date, and there are many photographs illustrating common diseases of the skin. There is, however, no mention of penicillin treatment, and we hope it will be included in the next edition.

HYGIENE.—By J. R. Currie, M.A. (Oxon.), M.D., LL.D. (Glas.), D.P.H. (Birm.), F.R.C.P. (Edn.), and A. G. Mearns, B.Sc., M.D., B.Sc. (Pub. Health), D.P.H. (Glas.), F.R.S.(E.). Second Edition. 1945. Pp. xv plus 432, with 89 figures in text. Publishers: E. and S. Livingstone, Ltd., Edinburgh. Price, 21s.; postage 7d.

The teaching of hygiene and public health was not long ago confined to a study mainly of water supplies, ventilation, food, sewerage, infectious diseases and vital statistics, and its importance to the practitioner of medicine was never sufficiently stressed on students. It now includes social services such as maternity and child welfare, school hygiene and mental hygiene. Industrial hygiene has come to the forefront, and the latest addition is the study of disease in the light of man's domestic circumstances and environment, or in other words, social medicine. It is perhaps no exaggeration to say that sanitary service has played an important part in the conduct of the present war. All aspects of the subject are presented in this book in an attractive and practical manner and within reasonable space. In the arrangement of the material, priority has been given to the social aspects of hygiene. This is the second edition of the book and incorporates changes caused by the war. It is written chiefly for medical students in Britain and hence contains many matters which are not yet applicable to Indian conditions, but it is good to know of them.

R. N. C.

PULMONARY TUBERCULOSIS: A HANDBOOK FOR STUDENTS AND PRACTITIONERS.—By R. Y. Keers, M.D. (Edn.), F.R.F.P.S. (Glas.), and B. G. Rigden, M.R.C.S. (Eng.), L.R.C.P. (Lond.). Publishers: E. and S. Livingstone, Ltd., Edinburgh. Pp. xii plus 273. Illustrated. Price, 17s. 6d.; postage 7d. (Home)

In this small book the authors have presented briefly but clearly the present position of pulmonary tuberculosis for the benefit of students and busy practitioners. As stated in the foreword by Dr. F. H. Young, they have kept in the foreground the fundamental conception that pulmonary tuberculosis is a generalized disease which becomes localized in the lungs for anatomical and physiological reasons. The book begins with a historical survey and then deals with the bacteriology, pathology and epidemiology of the

disease. These are followed by clinical chapters which are well illustrated by numerous x-ray photographs, many of which are from the Brompton Hospital and are accompanied by line drawings with the legends. Here the student will find that when he comes to put his knowledge into practice he will be amply repaid for the time spent in their study. In management, emphasis has been laid upon the treatment of the tuberculous patient as opposed to the tuberculous lung. In the chapter dealing with collapse therapy, the scope and limitations of each method have been clearly indicated, but more specialized details have been omitted. A chapter has also been devoted to 'after care'; in this connection the authors state that while the objectives of after-care are plain, there are great difficulties to be overcome; and the intrusion of economic factors confronts us with a problem which can be solved satisfactorily only by concerted action, in which the lead must come from the government. The book will prove useful to those for whom it is intended.

PATHOLOGY: AN INTRODUCTION TO MEDICINE AND SURGERY.—By J. Henry Dible, M.B. (Glas.), F.R.C.P. (Lond.), and Thomas B. Davie, B.A. (Cape), M.D. (L'pool), F.R.C.P. (Lond.). Second Edition. 1945. Pp. x plus 946, with 385 illustrations including 8 plates in colour. Publishers: J. and A. Churchill, Ltd., London. Price, 45s.

In this new edition the book has been considerably rewritten and includes recent advances of pathological knowledge, notably of such matters as crush injuries, hepatitis, shock and the problems arising from blood incompatibility. In addition, there are two new features—the one being a short section upon gynaecological pathology and the other a description of parasites and parasitic diseases. In presenting the subject, the authors have discarded the old conventional methods and taken pains to show how the disease processes go on in the living body and lead to certain consequences. The style is lucid and the illustrations are very good. It should be a popular textbook with students.

Abstracts from Reports

PENDRA ROAD SANATORIUM (C. P.). ANNUAL REPORT, 1943-44

THIS sanatorium which was opened in 1916 with only 12 beds has made excellent progress. It has now 155 beds and 76 members of staff and its annual budget is nearly a lakh of rupees. Its situation, climate and accessibility are ideal. During the year 177 patients were treated and discharged, of whom 138 were found to be suffering from pulmonary tuberculosis. Among these 138, 9 were early cases, 8 moderately severe, and 121 advanced cases. Ninety patients were discharged with positive results, viz, 10 as arrested, 47 as much improved, and 33 as improved. Eighteen were discharged as stationary, 13 as worse and 17 died. Chemotherapy, surgical treatment, x-ray and ultra-violet ray treatment are given.

Besides the treatment of patients it is also proposed to undertake training of doctors and health visitors. Among other extensions and improvements in view may be mentioned the provision of an after-care colony which will be the first of its kind in Northern India. This is already in its preliminary stage.

C.M.S. MISSION HOSPITAL IN SRINAGAR. ANNUAL REPORT, 1944

THE year 1944 has been a busy one in the hospital. Well over 48,000 visits were recorded in the out-patient department, an excess of more than 14,000 on the

figures for 1943. No less than 2,707 patients were admitted to the wards, and this constitutes a record for the hospital. It has been a busy year particularly for surgery, 816 major operations having been performed and 4,557 minor ones. All this reflects credit on the management, as the circumstances were abnormal. There was great shortage of staff and drugs and the supplies of linen and drugs were restricted. Incidentally, it is mentioned that for long ages Kashmir has been troubled with outbreaks of cholera, dysentery and typhoid. Cholera can usually be traced to pilgrims coming from the plains to the sacred cave at Amarnath. Dysentery, chiefly bacillary, is always present in Kashmir and typhoid is very common. The expenditure on account of the hospital is well over Rs. 60,000.

TATA MEMORIAL HOSPITAL FOR THE TREATMENT OF CANCER AND ALLIED DISEASES: FIRST TRIENNIAL REPORT, 1941- 1942-1943, BOMBAY

THIS hospital came into being in 1941, and the report covers the first three years of its existence. It appears that no efforts or expense were spared to make it an ideal hospital for cancer patients. During the three years, the Tata Trust has spent a sum of forty lakhs on building, x-ray, radium and other equipments. Even while plans were maturing, Indian students and doctors were sent for special training abroad. These men have returned and now hold important appointments on the staff.

The hospital has already gained a reputation among the medical profession as well as the general public, and patients are now being referred for diagnosis and treatment from all over the country. A high standard is being maintained. Details of the work done and results of the experience are summarized in the report. The hospital is certainly carrying out a much-needed service in the country.

THE TUBERCULOSIS ASSOCIATION OF INDIA. SIXTH ANNUAL REPORT, 1944

IN spite of prevailing adverse conditions progress has been made in the year under report. In addition to the thirty affiliated associations, two more are under formation in Bhopal and Gwalior and another is in contemplation in Bahawalpur. Eight clinics, four sanatoria and two hospitals were opened during the year. One clinic and one hospital are under construction, and proposals for the construction of two clinics and three hospitals are under consideration. As technical adviser, Dr. P. V. Benjamin devoted a considerable portion of his time to the affairs of the Association. One great difficulty that is being encountered is the dearth of tuberculosis workers; this is being met by holding post-graduate refresher courses and training health visitors, but for various reasons these courses had to be limited. The Mysore University has just introduced a T.D.D. course, and most probably Calcutta and Delhi will soon follow. There is already one functioning in Madras and it has become very popular. These courses will somewhat ease the problem of the supply of adequately qualified specialists for whose training opportunities in India are limited. Publicity and propaganda which is one of the main functions of the Association was carried on, within war-time restrictions, by means of charts, pamphlets and booklets, the sale of which fetched Rs. 4,300. It is hoped to introduce in the near future a fuller use of the screen and the microphone. The *Indian Medical Gazette* has been publishing a special tuberculosis number for the past seven years, but it is felt that the time has come when the Association should have a journal of its own.

The Lady Linlithgow Sanatorium at Kasauli treated 366 patients against 344 in the previous year. It had 190 beds of which 108 are reserved by Governments,

affiliated associations and others. War conditions have held up expansion. The New Delhi Tuberculosis Clinic treated 3,634 patients during the year; it has continued to play an important rôle by arranging home visits and contact examinations, training post-graduates, health visitors and nurses, and continuing the scheme of organized home treatment.

At the sixth annual general meeting of the Association, a deserving tribute was paid to Sir Cameron Badenoch, the honorary treasurer, on the eve of his retirement. He has been actively associated with the tuberculosis movement in this country for the past ten years. His experience and judgment have been of great value to the Association.

Correspondence

ENDEMIC FLUOROSIS IN WESTERN KWEICHOW

SIR,—In 1935 while he was staying at Stonegateway mission station in the extreme west of the province of Kweichow, Dr. Kilborn of West China Union Medical School, noticed the frequent occurrence of 'mottled enamel' amongst the tribes people of this area. He was also asked to see one or two people who were suffering from stiffness of the joints, especially in the spine. Suspecting the possibility of fluorine intoxication he took some samples of well water. They showed varying contents of fluorine, one specimen as high as 12 parts per million.

In 1941 the work was continued by Dr. T. S. Outerbridge then stationed at Chaotung, a city in Yunnan, one day's journey from Stonegateway. Outerbridge did a house-to-house examination of all the people in the village from whence the cases of 'poker back' originated. The investigation showed that nearly all the inhabitants had mottled teeth, and about six people were suffering from 'poker back', of various degrees. Further samples of water were sent for analysis, and showed fluorine contents varying from 6 to 13 parts per million. The source used by the people who showed the joint conditions contained 12 parts per million.

Dr. Outerbridge attempted to arrange for one of the advanced cases to be sent to Chengtu for x-ray and other investigations. Unfortunately just before he was due to leave, the patient fell from a boulder, not more than three feet high. His friends who were present said that he died in about two minutes.

Just over a year later, I visited the village and disinterred his remains. All the vertebrae from the second cervical together with the bones of the pelvis, and the ribs were fixed in their positions as in life. Actually there was a fracture at about the level of the eighth dorsal vertebra, so that the lower dorsal vertebrae, lower ribs, lumbar vertebrae and pelvis came out in one piece, the rest of the vertebrae and the upper ribs came out as another piece. The bones were held together by masses of new bone laid down in the joint capsules, ligaments and tendons. The costal cartilages were not calcified. The atlas had been fused to the occipital bone, and the odontoid process was fused into the arch of the atlas, and had been separated from the second cervical vertebra. The skull bones were thickened, but they were unusually fragile and the cranium was broken up into numerous fragments. The face bones were normal. The long bones showed numerous spiky exostoses, specially along the attachments of the interosseous membranes, and at the points of attachment of muscles. The joints showed osteophytes around their edges, but no erosion of the joint surface. The spinal canal showed gross narrowing, being not more than 1.2 cm. diameter at the second cervical and again at the eighth dorsal.

Further investigations especially of the teeth of school children have been carried out over a wide area. Some villages show 100 per cent of children affected, of those who spent the first four years of life in a contaminated spot. The condition is found to have a patchy distribution over an area measuring about 150 miles from north to south. So far, only one source has been found to produce the advanced bone and

joint condition, and that only after a minimum of about 30 years' residence. The whole area is extremely mountainous, and situated at about 6,000 feet above sea level. The rock appears to be mainly limestone.

The diet of the people consists mainly of maize, supplemented with potato, and very occasionally meat and green vegetables. The general standard of living is extremely low. The area is populated mainly by aboriginal tribes, but there are some Chinese living in the area, and they are equally affected.

So far the investigations are far from complete, and only a small number of specimens of water have been examined. However, there seems to be little doubt of the diagnosis of endemic fluorosis.

This is strictly intended as nothing more than a preliminary note. All the facts are quoted from memory as my records are not available. I also regret that I am not able to produce my photos of the cases and the skeleton. Further publication will certainly be made in due course.

OLIVER LYTH, M.R.C.S., L.R.C.P., L.D.S.

ERRORS IN DISPENSING DUE TO CONFUSION OF WEIGHTS

SIR,—Mistakes have been made in weighing out solids on account of mixing up the avoirdupois weights with the apothecaries', which does not appear to be uncommon in chemist's shops and in dispensaries. The dispenser is no doubt primarily responsible for such errors, but does this altogether absolve the prescriber particularly when his patient has to suffer for the error?

Let us take the instance of a patient of acute nephritis for whom 8 doses, each containing 30 grains of potassium acetate, have been prescribed. The total quantity of the drug to be weighed out for the purpose is 240 grains = 4 drams = $\frac{1}{2}$ ounce of the apothecaries' system. Instead of using several pieces of weights to make up the $\frac{1}{2}$ ounce, the $\frac{1}{2}$ ounce piece of the avoirdupois system, being more convenient to handle, is used with the result that only about 220 grains are taken for the 8 doses, and each dose then contains only 27 grains of the drug instead of 30 grains.

It is not uncommon that the $\frac{1}{2}$ oz. avoirdupois weight has been used to weigh out 120 grains of quinine sulphate for making 12 doses of a mixture of 10 grains per dose of the drug, and on testing the mixture with phosphotungstic acid solution it is found deficient in its quinine content, because the actual amount of the drug per dose is 9 grains and not 10 grains.

If the dispenser is in the habit of using avoirdupois weights, in making 16 doses of stock white mixture each to contain 'one dram' (intending 60 grains) of magnesium sulphate, he may weigh out one ounce with the result that each dose will contain only about 27 grains instead of 60 grains of the drug.

And worse is the luck when in making 24 doses of the stock quinine mixture, each to contain 10 grains of the sulphate the dispenser calculates 4 drams as equivalent to $\frac{1}{2}$ ounce (avoirdupois) and weighs out the drug accordingly, with the result that the mixture labelled as containing 10 grains of quinine sulphate

per dose does not contain even 5 grains, and therefore the patient continues to suffer when this mixture is administered. Actually this happened once when the patient was himself a medical man. The possibility of adulteration of the quinine sulphate was in this instance ruled out by testing a mixture of three doses freshly prepared with the stock powder weighed out in grains.

Fortunately the instances of mishandling or miscalculations given above lead to underdosing only, and in dispensing, the chances of overdosing with a reversal of calculations—a crooked process—are remote in practice. Errors have however been detected on checking stocks of solids when out of an ounce bottle actually containing 437.5 grains of calomel one dram of 60 grains was weighed out for use and the stock book was debited with one dram avoirdupois.

For easy reference the weights of the two systems are given below :—

Avoirdupois weights (Imperial system)

Commonly used in all ordinary trade dealings and the dosage of drugs in the British Pharmacopœia.

1 dram = 27½ grains
1 ounce (oz.) = 16 drams = 437.5 "
1 pound (lb.) = 16 ounces = 256 drams = 7,000 "

Apothecaries' weights (same as Troy weights)

1 dram (ʒ) = 60 grains
1 ounce (ʒ) = 8 drams = 480 "
1 pound = 12 ounces = 96 drams = 5,760 "

The masses of dram, ounce, and pound of the two systems are not the same.

The pieces of weights which are usually supplied with the balances in the market are :

For avoirdupois system = ½ oz.; ¼ oz.; 1 oz.; 2 oz.;
4 oz. or ½ lb.; 8 oz. or
1 lb.; and 1 lb.

For apothecaries' system = 1 gr.; 2 gr.; 3 gr.; 4 gr.;
5 gr.; 6 gr.; 10 gr.; 20 gr.;
30 gr.; 40 gr.; 60 gr. or
ʒi; and 120 gr. or ʒii.

For elimination of such mistakes the general practitioner would suggest the raising of the compounder's standard of training, but that alone would not justify his inaction to ensure accuracy in the dispensing of his prescriptions. What is he going to do when he can have no personal touch in the dispensing of his prescriptions?

X.

TRANSMISSION OF KALA-AZAR IN INDIA

SIR,—Much time has elapsed since Malone and Brooks' article appeared in the October 1944 number of the *Indian Medical Gazette* which argued serious doubt on the transmission of kala-azar by the sandfly.

Is there no one in India who can either corroborate or disprove the contentions made therein? One would have expected something from the officer in charge of the Kala-Azar Commission* by now.

The said letter (article) ought not to be allowed to pass as it seriously challenges the textbook teaching on the subject.

When those with all facilities for conducting inquiry of such an important matter 'keep mum' what is the ordinary G.P. to do? Will the officer suggested restore shaken faith?

B. I. BOUCHE, M.R.C.S. (Eng.),
L.R.C.P. (Lond.),
MAJOR, I.M.D. (Retd.).

'WISTERIA', MUSSOOREE,
20th June, 1945.

*The Kala-Azar Commission has ceased to exist.

Service Notes

APPOINTMENTS AND TRANSFERS

COLONEL S. L. BHATIA, M.C., was appointed as Officer on Special Duty under Director-General, Indian Medical Service, from the 19th April, 1945, to the 30th April, 1945.

Lieutenant-Colonel C. A. Bozman is appointed to officiate as Public Health Commissioner with the Government of India, with effect from the 1st April, 1945, *vice* Colonel E. Cotter, C.I.E., granted leave.

The services of Lieutenant-Colonel A. N. Chopra are replaced at the disposal of the Government of Orissa, with effect from the afternoon of the 5th May, 1945.

Major C. J. Hassett, M.B.E., is appointed Civil Surgeon, New Delhi, with effect from the 17th April, 1945.

Major T. C. Puri is appointed Deputy Public Health Commissioner with the Government of India, with effect from the 20th April, 1945.

Major M. Sendak has been appointed as Officer on Special Duty in the Home Department, with effect from the 28th April, 1945.

The undermentioned officer is transferred to the General Service Cadre, with effect from the date specified :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commission)

Captain Sasanka Sekhor Hazra. Dated 8th February, 1945.

The undermentioned officer of the Indian Medical Service reverts from the Indian Army Medical Corps and is seconded for service with the Royal Indian Navy.

Captain (T/Maj.) W. S. Empey. Dated 1st April, 1945.

The undermentioned I.M.S. (E.C.) officers revert from the Indian Army Medical Corps and are seconded for service with the Royal Indian Navy :—

Captain P. S. Clarke. Dated 23rd April, 1942.

Captain C. M. Bissett. Dated 5th March, 1942.

Lieutenant Krishan Kumar. Dated 15th March, 1945.

The undermentioned officer of the Indian Medical Service (E.C.) reverts from the R.I.N.V.R. and is seconded to the Indian Army Medical Corps :—

Surgeon Lieutenant-Commander P. B. Srivastava
Dated 1st April, 1945.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

To be Captains

Mohammed Abdur Rauf. Dated 5th February, 1944.

Fred Joseph Mendonca. Dated 9th January, 1945.

Shankar Mahadeo Tarkunde. Dated 1st February, 1945.

Shanti Swaroop Goyal. Dated 19th February, 1945.

Mukundan Madhusudan Tampi. Dated 12th February, 1945.

Vasant Vinayak Joshi. Dated 5th February, 1944.

Barin Deo Misra. Dated 12th March, 1945.

Moothedath Narayana Menon. Dated 15th March, 1945.

To be Lieutenants

George Henry Farran Humphreys. Dated 3rd April, 1943.

Michael Alexander Rozalla. Dated 19th February, 1945.

Mohd. Humayun Khan. Dated 15th February, 1945.

Abdurrahman Mohammad Khan. Dated 2nd February, 1945.

Harbhajan Singh Athwal. Dated 21st February, 1945.
Puthsala Dharmaraju. Dated 9th February, 1945.

15th February, 1945

Kodancha Vasudeva Rao.
Kuppa Venkata Subrahmanyam.
Vallary Venkateswara Surya Pratapa Rao. Dated 16th February, 1945.

19th February, 1945

Paravastu Srinivasachari.
Tunuguntla Balagangadhara Tilak.
Bommireddipalli Venkata Row.
Kunumilli Suryanarayana Rao.

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T. Shuwan Prakash Sharma.
Krishnaswami Gokhale. Dated 17th February, 1945.
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Kanneppadi Satyashankar. Dated 7th March, 1945.
Joginder Singh Patheja. Dated 3rd March, 1945.
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Nidumolu Sreeramamurthy. Dated 21st March, 1945.
Md. Abdul Majid. Dated 6th October, 1944.
Baidya Nath Ghose. Dated 9th October, 1944.
Aparba Kumar Ghosh. Dated 13th October, 1944.
Quazi Abul Khair Md. Abdul Khaleque. Dated 15th October, 1944.
(Miss) Gyan Sham Singh. Dated 1st February, 1945.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

(WOMEN'S BRANCH)

To be Captain

(Miss) Achy Mathew. Dated 19th March, 1945.

To be Lieutenant

(Miss) Ambika Kallat. Dated 17th January, 1945.

PROMOTIONS

The undermentioned officers are granted local rank of Brigadier without effect on pay and pension whilst employed as shown against each:—

Lieutenant-Colonel (A/Col.) S. M. Hepworth, I.A.M.C., Consultant Radiologist, G.H.Q. Dated 31st October, 1944.

Lieutenant-Colonel (T/Col.) M. M. Cruickshank, c.i.e., I.A.M.C., Consultant Surgeon, Southern Army. Dated 22nd March, 1943.

Major to be Lieutenant-Colonel

C. K. Lakshmanan. Dated 21st April, 1945.

Captains to be Majors

23rd April, 1945

A. W. Sampey. C. L. Greening.
J. Reidy. C. B. Jones.
S. N. Chatterjee. Dated 5th May, 1945.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
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(Emergency Commissions)

(WOMEN'S BRANCH)

Lieutenants to be Captains

(Mrs.) B. N. Akeroyd. Dated 25th October, 1944.
(Mrs.) J. E. Harland. Dated 13th January, 1945.
(Miss) D. M. Norman Jones. Dated 15th August, 1944.

RETIREMENTS

Colonel R. V. Martin, c.i.e. Dated 17th July, 1944.
Lieutenant-Colonel C. de C. Martin. Dated 7th August, 1944.
Lieutenant-Colonel G. A. Hildreth. Dated 5th April, 1945.

RELINQUISHMENTS

The undermentioned officer is permitted to relinquish his commission on grounds of ill health, and is granted the honorary rank of Captain:—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Captain S. K. Visveswar. Dated 18th February, 1945.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Captain (Mrs.) Saralabai Atma Ram Kulkarni, on grounds of ill health, dated 1st May, 1945, and is granted the honorary rank of Captain.

RESIGNATIONS

(Emergency Commissions)

Captain J. R. M. Johnson, dated 16th August, 1944, and is granted the honorary rank of Captain.

INDIAN MEDICAL SERVICE

Captain (Mrs.) G. O. W. Millington, dated 30th August, 1944.

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The Editors of *The Indian Medical Gazette* cannot advise correspondents with regard to prescriptions, diagnosis, etc., nor can they recommend individual practitioners by name, as any such action would constitute a breach of professional etiquette.

Original Articles

HYDATID CYSTS

A CLINICAL STUDY OF A SHORT SERIES.

By D. A. ANDERSEN, M.B. (Lond.), F.R.C.S. (Eng.)
 Chief Medical Officer, The Salvation Army Evangeline
 Booth Hospital, Ahmednagar

THE subject, hydatid cyst, is familiar to every student of surgery; it is a subject on which pathology books are expansive; and it is also rather a favourite subject with examiners: but from questioning medical associates in this area, I gather that they are not very commonly diagnosed in Western India, and it seems worth while to record a series of ten cases seen in the last four years, which, together, give a fairly comprehensive clinical picture.

Incidence.—In 1943, four cases were operated upon out of a total of 388 surgical operations (excluding minors), making 1 per cent of operation cases. On the average, however, two cases are seen a year, and this appears to be fairly constant, indicating that the condition is not very rare.

Occurrence in animals.—An enquiry from the local veterinary surgeon elicited the interesting information that he had on two occasions in the last year found hydatid cysts in the liver when post mortems had been requested because of unexplained death. One case was that of a buffalo which had been beaten heavily. At the post mortem the veterinary surgeon found several hydatid cysts in the liver, the largest being of the size of a mango, and of these at least two were ruptured and had leaked into the peritoneal cavity. Death was apparently due to acute anaphylaxis. In the other case the finding of the hydatid cyst appeared to be incidental.

He advanced the general information that hydatid cysts of the liver were seen only occasionally in slaughter-house inspections, chiefly in sheep, and rarely in goats and cattle. He could not give definite figures. He had no knowledge of the local incidence in dogs of *Tania echinococcus*.

Pathology.—The salient points are familiar, but some are recalled as they help in visualizing the clinical picture.

Tania echinococcus eggs are excreted in the faeces of the dog (the definitive host) in a developing state, the hexacanth or boring embryo. The egg is 30 to 36 μ in length.

On reaching the stomach of the intermediate host, usually sheep, occasionally man or cattle, the chitinous shell is digested, and the active embryo thus liberated bores into the mucous membrane of the small intestine and reaches a radicle of the portal vein, whence it is carried to the liver, being deposited near the hepatic surface on account of the terminal character of the blood vessels. Some ova apparently fail

to be arrested in the liver, and are stated to be carried to the lungs. Even here the ova may not be trapped, and then the general circulation is invaded, with the resulting development of cysts in any part of the body.

It is interesting that it has been recorded that ova are sometimes carried to the general circulation by the lacteals. This seems to afford an easier explanation of the entirely extrahepatic cases of which this series has four. It avoids the necessity of assuming the passage of a hexacanth five times the diameter of a red blood cell through the liver and lung capillaries, and, on the face of it, it does not seem more difficult for a boring embryo to find a lacteal than a portal radicle in the intestinal mucosa. The relative numbers of portal radicles and lacteals for instance, or some other physical factor, might provide an explanation why the majority find lodgement in the liver.

The remaining six cases were in, or arising from, the liver, and two of these had general dissemination in the peritoneal cavity, due to rupture of a primary liver cyst. One of these at operation was found to have numerous cysts on the surface of every viscus with a peritoneal covering, and also deeply embedded in the layers of the mesentery. In some cases the mesenteric cysts were so deeply embedded that access was difficult because of the mesenteric vessels. This is probably due to a mechanical burrowing during growth of the cyst.

The structure of the adult cyst is important in the consideration of treatment. It has three layers, the inner two of which (endocyst) are parasitic, namely, the germinal layer and the laminated membrane; and the outer layer (or ectocyst), which is adventitious, and due to the reaction of the tissues.

It may be noted that in every case operated on, numerous daughter cysts were found. It is stated that daughter cysts are rare in children, and also when the cyst occurs in a well-protected site, such as the brain or marrow cavity.

No case was observed in the lung, which is said to be the next commonest site after the liver.

Clinical features

The clinical features of each case are briefly recorded, in the order in which they were seen.

Case 1.—Male, age 35. Farm labourer.

Complaint: swelling in armpit. Examination showed a fluctuant non-tender swelling in the axilla, deep to the pectoralis major, about 5 inches in diameter. At operation a pocket was found to extend up to the first rib deep to the axillary vessels. Operation: marsupialization of the ectocyst after removal of as much as possible of the endocyst, and painting with 1 per cent formalin.

Case 2.—Male, age 35. Farmer.

A history was given of a swelling in the liver area for an indefinite period, which, one year previously, was followed by general abdominal pain and distension (rupture of liver cyst). Increasing swelling since with dyspnoea. The physical signs were of ascites and multiple nodules in the liver, which were at first considered to be malignant secondaries with general

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INDIAN MEDICAL SERVICE

Captain (Mrs.) G. O. W. Millington, dated 30th August, 1944.

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Original Articles

HYDATID CYSTS

A CLINICAL STUDY OF A SHORT SERIES.

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THE subject, hydatid cyst, is familiar to every student of surgery; it is a subject on which pathology books are expansive; and it is also rather a favourite subject with examiners: but from questioning medical associates in this area, I gather that they are not very commonly diagnosed in Western India, and it seems worth while to record a series of ten cases seen in the last four years, which, together, give a fairly comprehensive clinical picture.

Incidence.—In 1943, four cases were operated upon out of a total of 388 surgical operations (excluding minors), making 1 per cent of operation cases. On the average, however, two cases are seen a year, and this appears to be fairly constant, indicating that the condition is not very rare.

Occurrence in animals.—An enquiry from the local veterinary surgeon elicited the interesting information that he had on two occasions in the last year found hydatid cysts in the liver when post mortems had been requested because of unexplained death. One case was that of a buffalo which had been beaten heavily. At the post mortem the veterinary surgeon found several hydatid cysts in the liver, the largest being of the size of a mango, and of these at least two were ruptured and had leaked into the peritoneal cavity. Death was apparently due to acute anaphylaxis. In the other case the finding of the hydatid cyst appeared to be incidental.

He advanced the general information that hydatid cysts of the liver were seen only occasionally in slaughter-house inspections, chiefly in sheep, and rarely in goats and cattle. He could not give definite figures. He had no knowledge of the local incidence in dogs of *Tania echinococcus*.

Pathology.—The salient points are familiar, but some are recalled as they help in visualizing the clinical picture.

Tania echinococcus eggs are excreted in the faeces of the dog (the definitive host) in a developing state, the hexacanth or boring embryo. The egg is 30 to 36 μ in length.

On reaching the stomach of the intermediate host, usually sheep, occasionally man or cattle, the chitinous shell is digested, and the active embryo thus liberated bores into the mucous membrane of the small intestine and reaches a radicle of the portal vein, whence it is carried to the liver, being deposited near the hepatic surface on account of the terminal character of the blood vessels. Some ova apparently fail

to be arrested in the liver, and are stated to be carried to the lungs. Even here the ova may not be trapped, and then the general circulation is invaded, with the resulting development of cysts in any part of the body.

It is interesting that it has been recorded that ova are sometimes carried to the general circulation by the lacteals. This seems to afford an easier explanation of the entirely extrahepatic cases of which this series has four. It avoids the necessity of assuming the passage of a hexacanth five times the diameter of a red blood cell through the liver and lung capillaries, and, on the face of it, it does not seem more difficult for a boring embryo to find a lacteal than a portal radicle in the intestinal mucosa. The relative numbers of portal radicles and lacteals for instance, or some other physical factor, might provide an explanation why the majority find lodgement in the liver.

The remaining six cases were in, or arising from, the liver, and two of these had general dissemination in the peritoneal cavity, due to rupture of a primary liver cyst. One of these at operation was found to have numerous cysts on the surface of every viscus with a peritoneal covering, and also deeply embedded in the layers of the mesentery. In some cases the mesenteric cysts were so deeply embedded that access was difficult because of the mesenteric vessels. This is probably due to a mechanical burrowing during growth of the cyst.

The structure of the adult cyst is important in the consideration of treatment. It has three layers, the inner two of which (endocyst) are parasitic, namely, the germinal layer and the laminated membrane; and the outer layer (or ectocyst), which is adventitious, and due to the reaction of the tissues.

It may be noted that in every case operated on, numerous daughter cysts were found. It is stated that daughter cysts are rare in children, and also when the cyst occurs in a well-protected site, such as the brain or marrow cavity.

No case was observed in the lung, which is said to be the next commonest site after the liver.

Clinical features

The clinical features of each case are briefly recorded, in the order in which they were seen.

Case 1.—Male, age 35. Farm labourer.

Complaint: swelling in armpit. Examination showed a fluctuant non-tender swelling in the axilla, deep to the pectoralis major, about 5 inches in diameter. At operation a pocket was found to extend up to the first rib deep to the axillary vessels. Operation: marsupialization of the ectocyst after removal of as much as possible of the endocyst, and painting with 1 per cent formalin.

Case 2.—Male, age 35. Farmer.

A history was given of a swelling in the liver area for an indefinite period, which, one year previously, was followed by general abdominal pain and distension (rupture of liver cyst). Increasing swelling since with dyspnoea. The physical signs were of ascites and multiple nodules in the liver, which were at first considered to be malignant secondaries with general

carcinomatosis of the peritoneal cavity from some bowel primary, or a coarse cirrhosis. There were also several abdominal swellings which were difficult to define because of the ascites. Tapping was unsuccessful and he refused laparotomy. The general health, however, was better than would be the case in late secondaries or advanced liver damage. He returned after three months with more swelling, and many rounded masses were now clearly felt in the abdomen. He agreed to operation, and very numerous cysts of all sizes were found in the liver and throughout the peritoneal cavity. Complete removal of all was not practicable, but all the large ones and as many as possible of the small ones were incised through the ectocyst, and the endocyst removed complete. Post-operatively he did well, and there was relief from symptoms for 2½ years. He has recently attended again, in good general condition, with an incisional hernia at the lower end of the operation wound and one obvious mesenteric cyst the size of an orange. The liver enlargement is, if anything, less, and he has no ascites. He has consented to a second operation soon.

Case 3.—Female, age 17. Farm labourer.

Complaint: increasing swelling of the abdomen for three years. At first it was in the left loin and not painful, but it had gradually extended and was moderately painful. On examination it was found that the tumour extended from the left costal region to the left pelvis, crossed the midline anteriorly, and bulged the left loin. On pelvic examination it was felt in the left fornix. Its surface was regular, it was tensely cystic and dull to percussion.

It was at first taken to be a hydronephrosis, but this was disproved by a uroselectan x-ray examination, which showed a small deformed kidney shadow above the swelling with the ureter following a wide curve along the medial border of the tumour. The diagnosis being uncertain, it was approached at operation by the anterior route to give adequate room. The peritoneal cavity was opened through a left lateral incision, and the peritoneum was found to be reflected just to the left of the opening. A needle was inserted into the cyst through the peritoneum, and at first clear fluid was withdrawn. It was then pushed further in, and thick yellow pus was aspirated. In view of this, the opening in the peritoneum was closed, and the anterior incision closed in layers, and a lumbar incision was made. The usual innumerable cysts of all sizes were extruded, some of which contained clear and some purulent fluid. The ecto-sac was marsupialized and the wall swabbed with 1 per cent formalin. This patient returned fourteen months later for a different complaint and there was a soundly healed wound and no sign of recurrence.

Case 4.—Female, age 35. Farmer's wife.

Complaint: moderate pain in the epigastrium for one and a half years. Examination showed a curious fluctuating mass, the presenting part being about the size of an orange, in the epigastrium, moving with respiration, and also moving from side to side easily for about three inches to the right and left, rather like a pendulum, indicating a deep attachment. At operation its anatomical relation to the liver was very much like that of a huge gall-bladder (to the left of the normal organ), covered by peritoneum, with a distended 'fundus' and gradually getting narrower as it extended backwards and upwards on the inferior surface of the liver. Total excision was attempted but the 'neck' was so deep that this was given up in favour of incision and marsupialization.

Case 5.—Male, age 30. Village carpenter.

Complaint: noticed a hypogastric swelling for one month. No serious disturbance of bowels or micturition. Examination showed a broad tensely fluctuant swelling arising out of the pelvis, superficially resembling a distended bladder. P.R. there was a smaller fluctuant mass, the size of a lemon, felt high up in the anterior rectal wall, presumably the lower end of the swelling. Operation: extraperitoneal

marsupialization. The bladder was not exposed at operation.

Case 6.—Male, age 32. Farmer.

Complaint: small slightly painful swelling in the right epigastrium. On examination it was clearly a swelling projecting from the anterior surface of the right lobe of the liver, about the size of a walnut. Fluctuation could not be detected. General health good. On screening, the liver not raised, and the right diaphragm moved normally. At laparotomy the swelling was found to be cystic, and clear fluid was aspirated. A diagnosis of hydatid cyst was made, which was later confirmed by finding scolices and hooklets. On feeling the upper surface of the liver, separated by at least 4 inches of normal liver, was an irregular, lobulated, and not obviously cystic, swelling 6 inches by 4 inches in diameter. On this account a fairly extensive honeycombing of the liver was likely—the alveolar type of hydatid—and radical treatment was clearly impossible, so the anterior cyst was aspirated and 10 c.cm. of 1 per cent formalin injected. Post-operatively, aspirations and injections of formalin were continued weekly for about a month. Eight months later the patient complained of pain, and aspiration showed a small amount of pus, so a second operation was performed. This time no cyst was evident on the surface of the liver, but it was localized by a needle and the liver incised down to it, the opening being enlarged by a finger. There was not excessive bleeding, and, after the loculi had been broken down as much as possible with the finger, a wide tube was inserted and left in as long as there was any discharge. The wound healed in about fourteen days, and the pain was improved, although the patient still complains of discomfort; it is probable that further trouble may arise from the deeper parts of the lesion which could not be treated.

Case 7.—Boy, age 10. Villager. (Outpatient only.)

Complaint: large painless swelling in right upper abdomen. On examination the right lobe of the liver was enlarged greatly and contained a cystic swelling, in which a thrill could easily be elicited. The father refused admission for operation, and further investigations were not possible.

Case 8.—This was also seen as an out-patient only, at a village clinic.

Male, age 30. Labourer.

Complaint: abdominal swelling ever since the age of 10, which was vouched for by his father. General health good, and discomfort slight, but the increasing size was causing anxiety. Examination showed several distinct globular abdominal swellings, about the size of a grape fruit, in each of which separately a thrill could be felt easily. The character of the thrill was exactly the same as is felt in a tense ascites on flicking with one finger and appreciating the vibration some distance away with the other hand. No primary cyst could be felt in the liver, and there was no free fluid discovered. The patient was instructed to attend hospital, but has not yet done so.

Case 9.—Female, age 22. Weaver caste.

Complaint: swelling on the antero-lateral aspect of the upper third of the right thigh for 2 months. It increased in size, became painful and then burst, about three weeks before admission, extruding what the patient described as egg-shells, together with pus. It was treated with simple dressings and a course of sulphonamides by a private practitioner and it apparently healed and the discharge ceased. Four days before admission the swelling increased and on admission was about 4 inches in diameter. On examination the lump was firm, roughly globular; fluctuation was not detected, and it was attached to the deep tissues (muscles) but not to bone, and there was an adherent scar. Elsewhere the skin was free. Treatment: It was first aspirated and thin yellow pus was obtained. It was therefore incised and a large number of hydatid cysts, mostly the size of a grape, together with about 3 to 4 oz. of free pus was discharged. Some of the individual cysts contained clear fluid, some purulent.

In view of the accessibility it was decided that a total excision of the hydatid cyst in this case should be done. However, this proved less easy than was anticipated, and required a wide dissection of the upper third of the thigh. The ectocyst was loculated and surrounded by dense fibrous reaction up to a full $\frac{1}{2}$ inch in diameter, and the only way to remove it adequately was found to be removal of the whole of the upper third of the right vastus externus, showing the intermuscular sheaths and the main femoral nerve trunk as it divided into separate branches to the vastus group.

Before this fact was appreciated, some of the femoral nerve branches were picked up in a haemostat. They were, however, not divided except for the one to the vastus lateralis and the resulting quadriceps weakness is improving and is expected to recover fully, in the course of about 6 months. The leg was put into plaster in extension at first to rest the quadriceps muscle, but she is now walking without plaster and having electrical treatment. There is a saucer-shaped cavity which is healing from the bottom by granulation.

Case 10.—Male, age 45. Farm labourer.

Complaint: pain followed by swelling of right upper abdomen for six weeks. Examination showed a seriously ill man. He had a tender tense globular swelling of the liver extending 6 inches below the right costal margin and across the midline. No thrill detected. No ascites. He had diffuse bronchitis.

Blood count: Hb. 75 per cent, R.B.C. 3,770,000, W.B.C. 8,000, polymorphs 76, lymphocytes 24, eosinophils nil.

Within 24 hours of admission he had a temperature of 104.2 and he was taken to the theatre. A needle was inserted and thin pus was found. Examination of this was made at once and one definite hydatid hooklet was found. Therefore laparotomy was done under local anaesthesia. The abscess of the liver was obvious but there was no adhesion whatever of the liver to the anterior peritoneum. As delay in waiting for adhesion was not considered possible, a long strip of gauze was soaked in 1 per cent formalin, and packed several times round the most prominent part of the abscess, shutting it off from the rest of the peritoneal cavity. A stab incision was made and an enormous quantity of pus and cysts was discharged. A large bore tube was inserted and found to go right through to the posterior part of the liver, at least 7 inches. The wound was packed around the tube.

The fever subsided in 48 hours and the abscess drained freely. When the packing around the tube was removed after 7 days, the drainage area was well shut off by adhesion from the general peritoneal cavity and no evidence of general peritoneal infection had been observed. However, the man gradually went downhill, and developed anorexia, pharyngitis and glossitis; in spite of intravenous glucose, and liver injections and nicotinic acid he died 6 weeks after the operation from what was presumed to be liver failure.

Differential diagnosis

The series illustrates several of the varieties of hydatid disease, and for purposes of considering diagnosis, the following classification is suggested:—

1. Uncomplicated cysts:

- (a) Hepatic.
- (b) Extra hepatic.

2. Complications:

- (a) Rupture.
- (i) Acute anaphylaxis.
- (ii) Dissemination (usually in the peritoneal cavity).
- (b) Suppuration;

and the diagnosis of each group will be considered briefly.

1. Uncomplicated cysts.

The average clinical picture is of a person under 35, most usually in this series, but not always, a male, generally employed about a farm, in good general health, who complains of a tumour which is slowly growing and has been known to be present for years in most cases, but not giving rise to acute discomfort. On examination there is a tense spherical swelling which can be observed to have grown in the plane of least resistance, which usually means towards the surface of the body (or viscus). If it is superficial, a definite thrill is easily elicited. The skin over it is not attached to it or tender, nor is it attached to the surrounding tissues generally except in the case of origin from a viscus, when it may be sessile or attached by a pedicle.

(a) In the case of uncomplicated cysts in the liver, it has to be distinguished from *secondaries in the liver* (by the good general condition and the absence of any primary on careful search); from *coarse cirrhosis* by the good general condition again, and by the more irregular and hard surface in cirrhosis. The history and the Wassermann test may help.

(b) Uncomplicated extra-hepatic. Usually a cystic well-defined swelling as described above in any part of the body where such do not usually occur would give rise to a suspicion of hydatid cyst. No cases of the cysts in the brain or lung or bone have been encountered which would give rise to difficult diagnostic problems. However, it can be noted that the intense fibrosis around a hydatid in muscle proved misleading, and also that another case was reported to me by a colleague to have been diagnosed first as a cold abscess.

2. Complications.

(a) Rupture.

(i) *Anaphylaxis*.—In this series the danger of acute anaphylaxis is illustrated in the veterinary case.

(ii) *Dissemination in the peritoneal cavity*.—In differential diagnosis the possibilities of tuberculous masses in the abdomen and peritoneal carcinomatosis have to be considered. The chief difference lies in the good general condition, and the well-defined separate cystic masses as compared with the generally doughy feeling of a tuberculous peritonitis with or without irregular masses, or the hardness with irregularity of a carcinomatosis. If separate thrills can be felt as in case 8, the diagnosis can, I think, be regarded as certain. Ascites may be present in any of these conditions and obscure the diagnosis.

(b) Suppuration.

The differentiation of a suppurating liver hydatid from an amoebic liver abscess can be very difficult or impossible clinically. Both patients are very ill. A history of a pre-existing lump previously not painful suggests hydatid; but may often not be obtained. A

history of recent dysentery, if present, would suggest tropical abscess. Aspiration in a hydatid will give thin yellow pus, while from a tropical abscess it is a rich reddish brown. Microscopical examination, if fortunate, may, in the case of hydatid cyst, show a hooklet or hooklets or rarely scolices. In amœbic infection the finding of amœbæ is uncommon. If a hooklet is found, then clearly operation and drainage are indicated. If not, and if doubt remains, a course of emetine has an almost magical effect on an amœbic abscess without secondary infection. There remains an intermediate group where the pus is not typical of amœbic abscess and the condition does not clear up quickly with emetine, nor are hooklets or other definite signs of hydatid disease found. Here there is a valuable place for the Casoni test, but this has not usually been available. I treated two cases of this kind by repeated aspirations plus sulphonamides, and they eventually improved and left, but one was reported to have died soon after of recurrence. After the experience of case 10 of a hydatid suppuration in the liver, I suspect that they may also have been infected hydatids, and would now explore and provide open drainage. Even if they proved not to be hydatids, after the failure of an adequate course of emetine and several aspirations, open drainage would be good treatment.

A curious observation was made in case 3 that aspiration gave successively clear and then purulent fluid. This observation was repeated in cases 5 and 9, when immediately it led to the exclamation, "Another hydatid!" In both cases some daughter cysts contained clear and others purulent fluid. The purulent fluid was sterile on culture on one occasion when tested. It would be interesting to know whether this has been observed before, and has, in fact, any diagnostic significance. The value of it, however, is limited by the fact that transperitoneal aspiration of a suspected hydatid cyst from the surface is inadvisable, unless it is followed by laparotomy immediately when proof of hydatid disease is obtained, either by the suggested sign or the finding of hooklets.

Laboratory aids to diagnosis

These have practically not been available in this series. However, I used some clear hydatid fluid from case 6 for the Casoni test (that from sheep not being available) on the patient himself, 0.1 c.c. being given intradermally, and thinking it to be similar to the tuberculin test, I took readings at 48 and 72 hours with a negative result. This was surprising, and the technique was checked and it was discovered that the reaction was almost an immediate one. 0.3 c.c. was, therefore, injected intradermally, and within ten minutes there was a wheal 35 mm. in diameter, which gradu-

ally passed off but was succeeded by a diffuse redness 3 inches by 3 inches when seen at 24 hours. The control was negative.

The precipitin reaction (Welch and Chapman) was once attempted but was inconclusive, and the complement deviation reaction (Weinberg and Parva) was not attempted. These two tests would need a larger laboratory, but the Casoni test is clearly of clinical value in small hospitals, when hydatid fluid is available.

A recent textbook states that it can be obtained from Allen and Hanbury's, but the Calcutta office does not stock it.

Eosinophilia has not been found of diagnostic value. In case 2 when first observed it was 12 per cent, which might be significant, but when taken three months later before operation it was only 2 per cent. In case 5 there was no eosinophilia found pre-operatively. Case 3 showed 2 per cent before operation; a routine blood count taken a month after operation, however, showed 14 per cent. A high count may, therefore, be suggestive, but a normal, or low one, does not rule out hydatid disease.

Treatment

The ideal procedure might be expected to be complete excision, but even in a case on the limb it proved relatively difficult and unnecessarily mutilating. It should not be attempted if it involves any risk of deep bleeding, or of escape of the hydatid fluid into the peritoneal cavity.

Complete removal of the endosac through the laminated layer is perfectly satisfactory, and was carried out in the multiple abdominal cysts of case 2, the endocyst being removed intact after incision of the ectosac.

In large deeply-placed sacs full of daughter cysts, this also was not practicable, and the procedure generally adopted was to open the ectosac near the surface after carefully packing off and protecting the surrounding tissues with towels wrung out in saline, and on top of that placing gauze soaked in 1 per cent formalin. All daughter cysts were then removed carefully, and the endosac of the main cyst removed as fully as possible, and then painted with 1 per cent formalin swabs. The adventitious sac was then brought to the surface and marsupialized by stitching to the skin, this being the standard treatment in the majority of cases. It would be better still to marsupialize the sac before opening it, but that was not always possible. The cavity was packed and dressed daily, and irrigation with 1 per cent formalin was also carried out several times again. A purulent discharge resulted, which lasted in this series from two to six weeks. The packing was maintained until it was gradually pushed out by the diminishing size of the cavity.

In eight cases there was no serious reaction after operation, and no evidence whatever of anaphylaxis.

Follow-up

Cases 3 and 4 are known to have a healed scar and no recurrence. Cases 1 and 5 have not reported again, and are probably well. Case 2 returned in good general condition after 2½ years, with peritoneal recurrence, prepared for another operation. Case 6 is still under observation and may have further trouble. Case 9 is progressing well and a cure is anticipated. Case 10, the only death in the series, had extensive liver damage from which he did not recover.

Summary

A clinical series of hydatid cysts is presented, indicating the incidence, presentation, differential diagnosis and response to surgical treatment. Six cases were hepatic, with or without peritoneal dissemination, two extra-peritoneal abdominal and two in the limbs. The general picture is a benign one in the absence of complications, particularly rupture into the peritoneal cavity and suppuration. Rupture may lead to sudden death from acute anaphylaxis, or, at a later date, such a widespread dissemination in the peritoneal cavity that extirpation of the disease is impossible. Also, the alveolar type in the liver cannot be dealt with radically.

It is pointed out that it may be impossible to distinguish a suppurating liver hydatid from an amoebic liver abscess, and it is suggested that in those cases where a course of emetine and aspiration does not have an unmistakable and rapid effect, open drainage should be carried out, and that the frequency of such infected liver hydatids may be found to be greater than previously suspected.

A special sign is mentioned, namely, that on aspiration of a suspected cystic swelling the finding of first clear and then purulent fluid indicates hydatid daughter cysts, of which only some are infected while others remain uninfected. This aspiration is not to be carried out transperitoneally, unless immediately followed by laparotomy if positive.

The absence of anaphylactic phenomena is pointed out when adequate care is taken and treatment is by incision and open drainage with marsupialization of the adventitious sac.

AN OUTBREAK OF ENTERIC FEVER

By W. H. ST. JOHN-BROOKS, M.B. (Camb.), M.R.C.P.
LIEUTENANT-COLONEL, I.M.S.

DURING the period March to June 1944, 175 cases of enteric fever were admitted to a military hospital in a training area for Gurkha troops. The great majority occurred during one six-week period. Among the Gurkhas 162

cases occurred, the remaining 13 among other Indian troops.

The epidemiological aspect formed an interesting study, but is outside the scope of this note which deals with certain clinical features and treatment.

Type of case

Cases were divided on clinical grounds into four groups of varying severity, the group 4 being subdivided into (a) non-fatal and (b) fatal cases.

Group 1.—Thirty-nine cases. These were cases of short duration and mild course. The average number of days of fever was 11.6, of which only 8.5 days on the average were spent in hospital. Some cases had only 5 or 6 days' fever in all. The majority presented the clinical picture of mild enteric for a few days, and then suddenly became afebrile and symptom-free (figure 1); but a few had fever as the only sign, and the diagnosis was confirmed by a positive blood culture, Widal reaction, or in one case by the appearance of a typical rash.

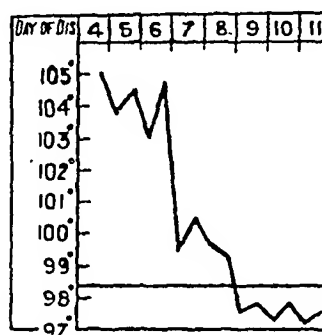


Fig. 1.—Group 1. Typhoid in an immunized subject. Severe onset with toxæmia and delirium. Crisis with disappearance of symptoms on 7th day. Blood cultures taken on 6th and 7th days grew *B. typhosus*.

The very much modified course of the cases in this group is almost certainly due to previous partial immunity. Its importance lies in the ease with such cases may be missed.

Group 2.—Forty cases. These also show the influence of previous immunization, usually with TAB. The average number of days of fever was

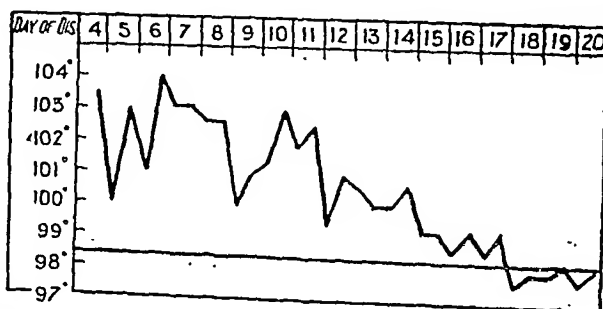


Fig. 2.—Group 2. Modified course of typhoid in a partially immunized subject. Blood culture taken on 6th day grew *B. typhosus*.

18.1, and the course was either mild throughout or definitely more severe with toxæmia, but terminating by very rapid lysis in the second or third week (figure 2).

Group 3.—Forty-two cases. These were more severe, and it cannot be said that they showed any evidence of immunity. Fever lasted on an

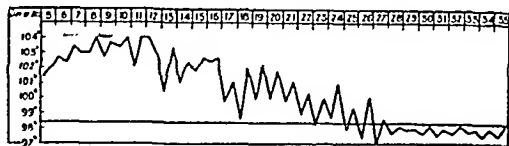


Fig. 3.—Group 3. Moderately severe course. No evidence of immunity.

average over 4 weeks (28.5 days) and the course approximated to a moderately severe classical one (figure 3).

Group 4.—Fifty-four cases, averaging 35.0 days of fever. All were extremely ill. Those who recovered (34 cases) had an average of 42.7 days of fever (figure 4). The 20 fatal cases averaged only 22.1 days of fever and it

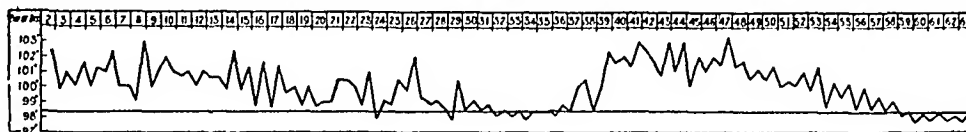


Fig. 4.—Group 4(a). Prolonged severe course with relapse, including hæmorrhage on 50th day.

was notable how deaths tended to occur early or not at all. Indeed if 5 cases (3 who died from perforation, 1 during relapse and 1 from paratyphoid A fever) are excluded, the average number of days of illness before death of the remaining 15 was only 16, of which only 13 days were spent in hospital. This is indicative of the toxic nature of the infection and the lack of immunity (figure 5).

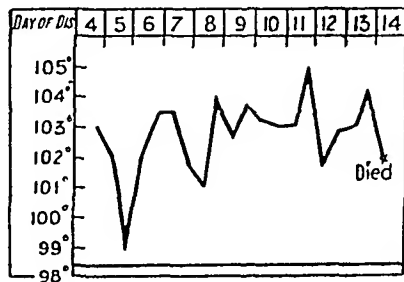


Fig. 5.—Group 4(b). Typical fatal case. Severe toxæmia and death on 14th day.

The clinical course of the disease in the 96 cases in groups 3 and 4 was comparable with that to be expected in unprotected people, and this impression was confirmed by the extreme toxæmia and early death of most of the fatal cases. There was other evidence also that in many cases TAB inoculation was incomplete or overdue.

Symptoms and signs.

A general account is given of the early stages and course. Owing to shortage of medical staff, it was not possible, particularly in the milder cases, to keep detailed records of all clinical observations. Attention was chiefly devoted to the seriously ill cases, but figures of the more important features and of complications are accurate and complete.

The early stages.—The average number of days of illness before admission was 3.8. In group 1, it was 3.1, in group 2, 3.9, in group 3, 3.9, and in group 4, 4.1. A Gurkha recruit rarely particularizes his symptoms very accurately. Only malaise, fever and headache were consistently mentioned. Abdominal discomfort or pain, diarrhoea, constipation, cough and epistaxis were mentioned occasionally but were not sufficiently striking features to be of value in early differential diagnosis. By contrast, the early signs were often almost conclusive. A majority even of the milder cases showed towards the end of the first week of fever the characteristic mental clouding, and the degree

of this was a good guide to the toxæmia and severity of the case. A furred tongue and bronchitis, mild or severe, have both been the rule and have proved definitely helpful in differentiating from other fevers in the early stages. In a community where malaria is so prevalent, a palpable spleen was of little help in diagnosis. Typical rose spots were observed in 14 cases, 8 of which were in group 4, and may have appeared transiently in other cases. The comparative insignificance of a rash on a dark skin accounts for this sign being of less importance than in Europeans, but surprisingly the appearance of a rash was several times useful in diagnosis. In one case the appearance of rose spots at the very end of a featureless febrile course of only a few days indicated that a blood culture (which proved positive) should be taken. A slow pulse was also a usual and useful finding, but a rapid pulse must not be regarded as definitely ruling out a diagnosis of enteric, as it was an occasional finding in toxic cases where heart and circulation were affected.

The course.—The cases in groups 1 and 2 slowly or rapidly became afebrile and symptom-free in the second or third week. In cases of groups 3 and 4, the notable features were the toxæmia and mental clouding of degree varying up to delirium and the typhoid state. The tongue cleared with defervescence, the bronchitis usually considerably earlier. Tympanites occurred only in one case, just before death.

Diarrhoea and constipation were never troublesome. The former did not require reduction of diet, and the latter was easily dealt with by enemata.

In severe cases, fever and toxæmia often persisted for weeks. In a few, intermittent fever occurred and must not be regarded as impossible in enteric (figure 6). Early in the

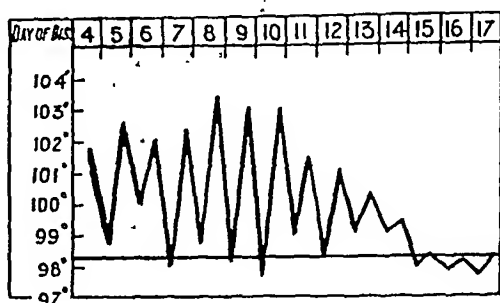


Fig. 6.—Intermittent fever in an immunized subject. Blood culture taken on 7th day grew *B. typhosus*.

course of a very toxic case, peripheral circulatory failure was common. Intravenous fluids sometimes gave improvement, but this group included most of the fatal cases. In one case, meningism was noted with a normal cerebro-spinal fluid.

There were no other notable symptoms or signs. The lack of troublesome symptoms is paralleled by the low incidence of complications mentioned later, and both may have been largely due to the diet given.

One case of miliary tuberculosis was provisionally diagnosed as enteric before the development of meningeal signs clarified the diagnosis. The earlier stages were almost indistinguishable. Two cases of kala-azar were similarly admitted to the typhoid ward in error.

Relapses.—Thirteen patients had relapses, a case incidence of 7.4 per cent.

In groups 1 and 2 there were no relapses.

In group 3, four cases had relapses. The number of days of each fever period is shown below. The number of days without fever which intervened is shown in brackets:—

Case A	..	20	(6)	21
" B	..	21	(4)	11
" C	..	21	(2)	12
" D	..	22	(3)	10

In group 4, six cases had 1 relapse each:—

Case E	..	31	(4)	23
" F	..	13	(2)	12
" G	..	16	(4)	20
" H	..	17	(3)	17
" I	..	19	(3)	18 (died)
" J	..	19	(4)	30

Three cases had 2 relapses each:—

Case K	..	12	(4)	26	(22)	12
" L	..	14	(3)	8	(4)	70
" M	..	53	(10)	11	(7)	23

One case died during a relapse.

On the whole, relapses were milder than the initial phase of fever, but there were notable exceptions, e.g. cases I and L.

Complications. (1) *Hæmorrhage*.—One case only had a hæmorrhage which occurred during a relapse. There was a little further bleeding next day, but blood transfusion was unnecessary and the patient recovered.

(2) *Perforation*.—Four cases had perforation, three of which occurred on the 18th, 38th and 36th day of illness. The former two died, the first after a long post-operative course. The fourth case was a 'sweeper' who had ambulant typhoid for one month in the lines and was admitted to hospital with general peritonitis. Post mortem showed two typhoid ulcers only, one of which had perforated.

(3) *Broncho-pneumonia*.—Thirteen patients developed broncho-pneumonia, generally as an extension of the initial bronchitis. Of these, 10 cases were in groups 3 and 4. A point I have previously noticed was that sulphapyridine often temporarily brought the temperature down to normal.

(4) *Minor conditions*.—One case developed submaxillary adenitis, one a small abscess of thigh, and another, with repeated epistaxis, had a maggot infestation of his nose which cleared on treatment. There were 2 cases of parotitis; one was a terminal event in a fatal case, and another occurred unexpectedly in a mild case with a clean mouth. It subsided without incision. One case developed a bed-sore.

Intercurrent diseases.—The stay in hospital was unduly prolonged on account of local conditions unconnected with the actual disease. This gave plenty of opportunity for the development of other illnesses.

Malarial relapses occurred in 24 patients, of whom 18 were in groups 3 and 4. Kala-azar was found and successfully treated in 4 patients. One case was admitted with mumps and another case developed mumps in hospital.

Other intercurrent conditions were one case each of pleural effusion, lymphogranuloma inguinale, bacillary dysentery, scabies, polyserositis and miliary tuberculosis. The last two conditions were fatal after recovery from typhoid was established.

Fatal cases

There were 20 fatal cases, a case mortality of 11.4 per cent. Three patients died after perforations, including one admitted with general peritonitis. Two others died after a prolonged course on the 40th and 48th days of the illness. The former died during a relapse, while the latter was a middle-aged 'follower' of poor physique, whose infection was paratyphoid A.

The other 15 cases averaged 16 days of illness each, and were marked by the early and profound toxæmia, which was in some cases during the first week comparable to that of typhus at the same stage. Death at this stage was the rule. It was thought that the full diet, given prevented deaths in the later stages from exhaustion and emaciation. Diet would be

expected to have little influence on the type of patient who died in the early stages (unless adversely, by precipitating hæmorrhage and perforation) and most of the fatalities fell into this class.

Post mortems emphasized the importance of the toxæmia, which was greater the earlier the day of death. The liver showed toxic focal necrosis, while the small bowel showed intense congestion with enlargement and engorgement of lymphoid tissue, which in the earliest cases showed practically no ulceration. Enlargement and deep congestion of mesenteric lymph glands was also a constant finding.

Diet

The principle of giving as full a diet as possible was adopted to prevent the wasting and weakness inevitable on a prolonged fluid diet. This principle is, of course, no innovation; but it is worth emphasizing because its value, at least in India, is by no means fully appreciated by either medical or nursing staff.

The following diets were worked out as standards from items included in the standard scales of hospital diet for Indian troops, and known to be always available.

Diet 1.—Initial diet. Calories 1,760 (approx.).

Milk	.. 40 oz.	Barley water.
Cream	.. 2 oz.	Chicken essence.
Sugar	.. 4 oz.	Vitogen (Horlick's substitute).
Egg	.. 1	Lemon, lime or orange juice.

Notes.—Feeds to be 2 hourly. 8 a.m. to 8 p.m. Not more than 6 oz. milk at a feed. Total fluid intake not less than 5 pints daily.

Diet 2.—Intermediate diet. Calories 3,560 (approx.) when the full diet is taken.

Milk	.. 60 oz.	Rice	.. 4 oz.
Cream	.. 2 oz.	Potatoes	.. 4 oz.
Eggs	.. 2	Chicken or fish	4 oz.
Bread	.. 4 oz.	Barley water, chicken essence, Vitogen, Vegamite.	
Butter	.. 2 oz.	Lemon, lime or orange juice.	
Fresh fruit	.. 8 oz.		

Notes.—Bread and butter to be cut thin. Potatoes mashed. Chicken minced. Some milk to be given as dahi (curd) or as rice pudding. Fruit to be given only when suitable (*i.e.* banana, papaya or mango, not orange or pomegranate). Feeds to be 2-3 hourly.

Diet 3.—Convalescent diet.

The ordinary hospital convalescent diet is given when the patient is afebrile.

Only severe cases in the early stages were given diet 1, while feeding was difficult. In all cases the full scale of diet 2 was reached as soon as possible, but the transition was made gradually according to the orders of the medical officer.

From the basis of these diets the following menus were evolved with the addition of extras available from time to time. It is difficult to provide a variety in designing Indian diets as there are fewer items available for selection than in British diet scales.

Typhoid menus

1. Initial diet.—2 hourly feeds.

Milk, alone or in combination with cream, Vitogen (Horlick's substitute), chicken essence or an egg flip. Sweetened fruit drinks in between feeds.

2. Intermediate diet.

8 a.m. Tea and biscuits, or milk.

10 a.m. (1) Milk, Vitogen or fruit drink and sugar, and (2) bread and butter with treacle, cream cheese or Vegamite.

12 noon. (1) Fish, pounded and boiled, or steamed, minced chicken, liver, or scrambled or lightly boiled eggs, and (2) mashed potatoes and butter, rice and strained dal, or rice pudding and golden syrup.

2 p.m. Milk, Vitogen or fruit drink and sugar.

4 p.m. (1) Fruit salad with sugar and cream, and (2) milk or dahi.

6 p.m. (1) Milk, cocoa or Vegamite, and (2) poached or scrambled eggs, custard or mashed potato with butter and milk.

8 p.m. Milk, Vitogen or fruit drink and sugar. Fluids and fruit drinks freely between feeds. Sweets to suck.

3. Convalescent diet.

Menus as for other convalescent patients.

It should be noted that none of the patients was vegetarian. Modifications in the diet would be necessary for patients who did not eat meat or eggs.

In fact very few cases had to be kept on diet 1 for more than a few days. Most patients were able and indeed eager to take the greater part of diet 2 on admission, and the full scale was attained as soon as possible.

It is worth noting, but should not perhaps be overstressed, that several out of the comparatively small number of fatal cases and cases with major complications occurred among the few cases in which feeding was difficult from the start and remained so in spite of every persuasion. The single case of hæmorrhage fell into this category, as also did one case complicated by perforation, the case whose second relapse lasted 70 days, the case of the middle-aged 'follower' who died on the 48th day and the only case in which developed a bed-sore. In all these there was a deterioration which was quite notable on comparison with those, however toxic, taking the full diet. In the latter, a good state of nutrition and general physical condition were maintained even in patients whose fever lasted many weeks. It seems reasonable also to ascribe to the diet the low incidence of troublesome symptoms and of complications, as there was no lack of severe cases and there was no other special treatment. There was, however, no control series.

Treatment

Apart from diet, the only routine treatment was that involved in careful nursing which was of a high standard. Little symptomatic treatment was necessary.

Intravenous glucose saline by continuous drip was given to a number of serious cases, toxic and dehydrated. Slight improvement sometimes followed, but this measure was rarely sufficient to turn the scales in a serious case.

Convalescent plasma or serum in quantities of 400 c.cm. was given to 7 patients, all very seriously ill; one died. Variable improvement both subjective and objective occurred in the others, but the series is too small for conclusions to be drawn.

Laboratory findings

Adequate laboratory investigations were impossible owing to shortage of laboratory equipment and staff.

B. typhosus was isolated from the blood on 93 occasions and *B. paratyphosus* A on 2 occasions. The percentage of positive blood cultures increased with the severity of the disease.

A careful analysis of all the results of Widal reactions has been made, but it has not been possible to correlate a rise in titre with either the stage of or the severity of the disease. Mild and severe cases showed both high and low titres both early and late in different cases. Some maintained a high titre for weeks; in others it fell away extremely rapidly.

Example.—Case N. Day 16. TO-1/320

Day 20. TO-1/320

Day 28. TO-1/320

Day 35. TO-1/640

Case O. Day 10. TO-1/1280

Day 18. TO-1/80

Routine clearance tests were done on all cases before discharge. Only one case showed a temporary carrier state, with a positive urine culture of *B. typhosus*. Three weeks later when the clearance tests were repeated, all cultures were sterile.

Disposal

Owing to the full diet given, patients who recovered, had, by the time they were afebrile, little or no lost ground to regain, and by the time clearance tests were complete were fit for discharge. A small minority were sent to a convalescent depot, but ultimately all cases returned to full duty.

Summary

A brief account is given of the clinical aspects of an epidemic of 175 cases of enteric fever in a Gurkha training centre.

Two points are commented on. The low incidence of troublesome symptoms and complications and the principle adopted of giving as full a diet as possible from the start of the illness.

The conclusion that there is an association between these two features is tentatively drawn.

I am grateful to Colonel B. E. Schlesinger for advice and encouragement, and to Lieut.-Colonel J. G. Stonham and the D.M.S. in India for permission to submit this note for publication.

STUDIES IN RINGWORM

PART II

THERAPY OF TINEA CAPITIS BY GONADOTROPIC HORMONES

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and

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TREATMENT of tinea capitis (ringworm of the scalp) in children has always been unsatisfactory. The multiplicity of the drugs used and the procedures mentioned in the textbooks make it difficult to formulate a routine method of treatment. Local antiseptics by themselves are not of much value, as the drugs cannot penetrate the skin to the root of the hair and control the infection inside the hair follicles. The infection can be got rid of by epilation of the diseased hair, but that is a difficult task, and children have been subjected to many painful and even hazardous methods to achieve this. Treatment with thallium acetate by mouth—a toxic drug—or epilation by x-rays by inexperienced operators, has been the cause of many serious accidents.

Tinea capitis is essentially a disease of children, and there is always a tendency to spontaneous cure at puberty. The disease is rare in adults. This observation is explained by some structural change in the hair produced by the gonadal activity at puberty. The development of the adult type of cell in the vagina of children by the administration of estrogenic hormones has been demonstrated, and the fact has been taken advantage of in the treatment of gonorrhoeal vulvovaginitis of children by oestrogenic hormone. Whooping cough, which is primarily a disease of children, has similarly been successfully treated by gonadal hormone therapy.

The above analogy led us to try gonadal therapy in the treatment of tinea capitis. This report is based on the treatment of 23 cases, and the result of this experiment, though not conclusive, is encouraging.

We were handicapped regarding the choice and supply of drugs owing to the present war conditions. A few hormone preparations for parenteral use were available and none for local use.

The drugs used were:—

1. 'Antuitrin S' (Messrs. Parke Davis & Co.)—Anterior pituitary-like gonad-stimulating hormone obtained from urine of pregnancy, 100 rat units per c.cm.

2. 'Ovocyclin' (Ciba)—The chemically pure follicular hormone oestradiol and its dipropionate ovocyclin P.

3. Perandren—Testosterone propionate (Ciba).

Diagnosis

In every case the clinical diagnosis was confirmed by microscopic examination, and the type of infection was determined by culture.

Of the 23 cases, 12 cases were of *M. audouini* infection, 6 cases were of *Tr. violaceum* infection and 5 cases were of *Tr. crateriforme* infection.

Therapy

One c.cm. of the drug selected was injected intramuscularly twice a week; an average of

10 injections was given to each patient in 5 weeks. Some patients received 12 injections. A few patients refused to continue after 7 or 8 injections. Children less than 8 years old received 0.5 c.c. as the first two doses.

The cases were divided in two series. In the first series the patients received only the hormone therapy and no other local treatment besides washing the scalp twice weekly with soft soap and spirit. In the second series, along with the hormone therapy and the wash, the

TABLE I

Eleven cases treated with hormones only and no local antiseptic used

Sex	Age	Condition on admission	Drugs used	Number of injections	Total quantity	Time taken, weeks	Result
<i>Microsporium audouini</i> INFECTION 6 CASES							
M.	10	Two big patches each more than one inch in diameter.	Antuitrin S.	10	10 c.cm.	5	Slight improvement.
M.	10	Two big patches	Do.	11	11.25 c.cm.	5½	Do.
F.	9	One big and three small patches	Do.	13	13 c.cm.	6½	Cured.
M.	6	Two big and four small patches of many months.	Ovocyclin	8	7 c.cm.	4	No improvement.
F.	5	Multiple patches of different sizes	Do.	12	11 c.cm.	6	Do.
F.	9	Two big patches	Do.	12	12 c.cm.	6	Cured.
<i>Trichophyton crateriforme</i> INFECTION 2 CASES							
F.	9	Multiple patches of various sizes	Antuitrin S.	10	10 c.cm.	5	Improved.
F.	11	Do.	Ovocyclin	10	10 c.cm.	5	No improvement.
<i>Trichophyton violaceum</i> INFECTION 3 CASES							
M.	10	Multiple small patches	Perandren	11	11 c.cm.	5½	Improved.
M.	8	Do.	Do.	10	9 c.cm.	5	Slight improvement.
M.	10	Do.	Do.	10	10 c.cm.	5	Do.

TABLE II

Twelve cases treated with hormone together with local antiseptics
Phenyl-mercuric-nitrate (Merfenal—May & Baker) ointment 1/1000

Sex	Age	Condition on admission	Drugs used	Number of injections	Total quantity	Time taken, weeks	Result
<i>Microsporium audouini</i> INFECTION 6 CASES							
F.	7	One big and three small patches	Ovocyclin	11	10 c.cm.	5½	Improved.
F.	7	One big patch	Do.	10	9 c.cm.	5	Cured.
M.	8	Three big and two small patches	Do.	10	10 c.cm.	5	Do.
M.	10	Four medium patches	Antuitrin S.	10	10 c.cm.	5	Improved.
F.	8	One very big patch 4 × 3 inches	Do.	11	11 c.cm.	5½	Cured.
F.	6	One big and three small patches	Do.	10	9 c.cm.	5	Improved.
<i>Trichophyton crateriforme</i> INFECTION 3 CASES							
F.	13	Two big and one small patches	Ovocyclin	10	10 c.cm.	5	Cured.
F.	7	Seven patches of different medium sizes.	Antuitrin S.	10	9 c.cm.	5	Do.
F.	13	Multiple small patches	Do.	10	10 c.cm.	5	Do.
<i>Trichophyton violaceum</i> INFECTION 3 CASES							
M.	13	Multiple small patches	Perandren	10	10 c.cm.	5	Cured.
M.	8	Do.	Do.	10	9 c.cm.	5	Not cured.
M.	10	Do.	Do.	10	10 c.cm.	5	Do.

TABLE III
Analysis of cases cured

Number of cases	Age	Sex	Type of infection	Drug used	Time taken, weeks	Local treatment
1	9	F.	<i>Microsporum audouini</i>	Antuitrin S.	7	Nil.
2	9	F.	Do.	Ovocyclin	6	Nil.
3	7	F.	Do.	Do.	5	Phenyl-mercuric-nitrate ointment 1/1000.
4	8	M.	Do.	Do.	5	Do.
5	8	F.	Do.	Antuitrin S.	5	Do.
6	13	F.	<i>Trichophyton crateriforme</i>	Ovocyclin	5	Do.
7	7	F.	Do.	Antuitrin S.	5	Do.
8	13	F.	Do.	Do.	5	Do.
9	13	M.	<i>Trichophyton violaceum</i> .	Perandren	5	Do.

TABLE IV
Comparison by sex

Total number of cases treated in each group	Number of cases cured	Number of failures	Type of infection	Male			Female		
				treated	cured	failure	treated	cured	failure
12	5	7	<i>Microsporum audouini</i> .	5	1	4	7	4	3
5	3	2	<i>Trichophyton crateriforme</i> .	0	0	0	5	3	2
6	1	5	<i>Trichophyton violaceum</i> .	6	1	5
Total 23	9	14		11	2	9	12	7	5

patients were given a good rub daily with an ointment containing 1 to 1,000 phenyl-mercuric-nitrate. The results are tabulated.

Analysis

From tables I and II we find that hormone therapy together with local antiseptic treatment gives better results than the hormone therapy alone and in treating a case of ringworm of the scalp one should make use of all the available measures.

From table III we find that *Microsporum audouini* and *Tr. crateriforme* infections responded better; this is perhaps explained by the fact that both these infections are confined to children and are very rare after puberty. Spontaneous cure at puberty is common in these infections. *Tr. violaceum* infection however is quite common in adults, causing sycosis barbæ, and in this country pustular folliculitis of the secondary sex hairs. Moreover trichophyton infection often persists even after puberty.

From table IV it is seen that female children responded better than male children and the older the children the better was the response. This was as expected.

Summary

1. Twenty-three cases of ringworm of the scalp were treated with the administration of gonadotropic hormones.

2. Some cases responded well to the treatment. Of these *Microsporum audouini* and *Trichophyton crateriforme* infections responded better than *Trichophyton violaceum* infection.

3. Female children responded better than male children.

4. Local antiseptics should be applied along with the hormone therapy.

[The advisability of using sex hormones for treating ringworm in children is open to question. It is not clear why oestradiol was given to some boys.—EDITOR, I.M.G.]

THE TREATMENT OF PLAGUE WITH SULPHATHIAZOLE

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AFTER a lapse of eight years, an outbreak of bubonic plague took place in Karnal district in 1944. The disease started on the 25th March as a result of importation from the Saharanpur district of the United Provinces, and lasted through the spring till the 26th May; it then broke out again at the end of October, on the reappearance of favourable climatic conditions,

and remained till the 9th December. During all this time the epidemic was responsible for 120 cases with 50 deaths, and occurred in one small town and eleven villages situated in a tract contiguous to Saharanpur district.

Out of 120 patients, 81 were given sulphathiazole treatment, under the general guidance and advice of the senior writer. Actual treatment was however given by the junior writer who also carefully recorded all observations and prepared case notes of each patient. All the patients were treated either in their homes or in huts in the fields, where their families had been evacuated.

No discrimination or selection was made among the patients in giving this treatment. There were however some to whom no treatment could be given owing to early death. Some others vehemently and persistently refused to take our treatment, and preferred to be attended by hakims or quacks. Excepting these, every other patient was put on sulphathiazole as soon as he was brought to notice, irrespective of the severity or the stage of his illness.

The routine treatment adopted in these cases was such as could be carried out in the homes of the patients, and consisted chiefly of sulphathiazole administered by the oral route, combined with a mixture of sodium bicarbonate and aromatic spirits of ammonia. In most cases this drug was given in the form of 'cibazol' tablets. It was started with an initial dose of 2 grammes followed by a maintenance dose of 1 gramme every 4 hours, making a total of 7 grammes in the first 24 hours. On the second and third days, the dose was reduced to 4 grammes, i.e. 1 gramme every 6 hours. This was further reduced to 3 grammes from 4th to 6th day, making a total of 24 grammes as the basic standard dose.

Children of the ages 8 to 14 were given half the above dose, and in smaller children, the dosage was correspondingly reduced.

In patients with a tendency to nausea and vomiting, one tablet of nicotinic acid was given about 15 minutes before each dose of cibazol. For combating toxæmia, soluseptasine 10 per cent solution and glucose 15 c.cm. of 25 per cent. solution were administered daily by the parenteral route. For cardiac weakness, tincture of digitalis was added to the mixture, while coramine was administered whenever cardiac failure was apprehended.

This group of 81 cases comprised the following types of plague:—

Bubonic	69
Septicæmic	3
Hæmorrhagic	2
Adenitis with severe gastro-intestinal disturbances	7

Seven cases developed complications during treatment; thus two had secondary pneumonia, two pregnant women had abortions, while three patients developed aphasia, which lasted two to six weeks after recovery.

Seventeen out of the 81 cases proved fatal. These included the 3 cases of septicæmic plague and 6 others in which this treatment was either taken up late, i.e. on the 3rd or 4th day of illness, or was not given fully in the prescribed dosage.

Eleven out of 81 were previously protected by anti-plague inoculations, and one of these eleven succumbed to the disease. The chief features noticed under this treatment were as follows:—

1. If the administration of the drug commenced on the first day of illness or immediately on the appearance of the bubo, and the drug was pushed in the prescribed dosage, the patient invariably became afebrile on the 3rd or 4th day, and the bubo gradually subsided in a week or 10 days.

2. If sulphathiazole was stopped at the initial improvement on the 3rd or 4th day, the pyrexia appeared again and the pain in the bubo reappeared with increased tenderness, when the drug had to be continued for a longer period, till the patient became afebrile again. In such cases the bubo invariably suppurated, and had to be incised.

3. The drug was of no avail in septicæmic cases, and all the 3 cases of this variety succumbed, in spite of every effort. The two hæmorrhagic cases, though severely toxic in the beginning, were cured under the treatment. Out of the 2 cases which developed secondary pneumonia, one recovered and the other died.

4. The drug should always be given with sodium bicarbonate, and in toxic cases soluseptasine and glucose should be given by the parenteral route. In cases with persistent nausea and vomiting, it is necessary to reduce the dose of the drug.

5. The case mortality among the 'treated' was 21 per cent. Even leaving aside the 11 inoculated persons, the deaths among the remaining 70 uninoculated were 16, giving a mortality rate of 23 per cent. On the other hand the total number of persons who did not receive cibazol treatment was 39, and among these 33 deaths occurred. They belonged to the following categories:—

	Cases	Deaths
1. Seen after death	9	9
2. Treated by hakims or quacks	17	16
3. Treated with stimulant mixture with tincture iodine due to non-availability of cibazol at the time	13	8
	39	33

Leaving aside the untreated, the mortality among the remaining 30 comes to 80 per cent.

The value of sulphathiazole in the treatment of plague has already been widely recognized and its use is advocated by Sokhey and others. The chief interest in publishing these results, however, lies in the fact that this was the first field trial of this medicine on such a scale in the rural areas of the Punjab. The unusually

favourable results obtained suggest that this procedure might profitably be adopted by other public health field workers who may be called upon to deal with epidemic conditions prevailing simultaneously in a number of scattered villages, rendering institutional treatment impracticable. In the circumstances, a method which can be carried out by the patients' relations under the directions of the medical officer, and which is known to be of proved therapeutic value, is sure to be highly advantageous both from the curative as well as prophylactic points of view.

The following are some of the case notes from the epidemic under discussion :—

(a) *Bubonic*—

1. A female, aged 20, unprotected, with an inguinal bubo, was seen on the first day of her illness with temperature 105°F., eyes bloodshot, tongue dry, pulse 120 to 130, respiration 32, face anxious. Cibazol treatment started at once, along with sodium bicarbonate, stimulant mixture, soluseptasine daily intramuscularly for the first 3 days. The temperature gradually came down by lysis on the fourth day and the bubo subsided on the 7th day. Convalescence was uneventful.

2. A Hindu male, aged 25, unprotected, had a bubo in the left groin with a temperature of 103°F. and great prostration. He was put on cibazol and stimulant mixture. The temperature fell to 99°F. on the 3rd day when he stopped taking cibazol. It went up again to 101°F. on the 5th day and swelling and pain reappeared in the bubo. He was put on cibazol, which was kept up for another 6 days, when the fever finally left him. The bubo however suppurated and had to be incised and dressed with sulphonamide powder.

(b) *Cases with gastro-intestinal disturbances*—

3. A Hindu male, aged 32, protected by anti-plague inoculation on the 7th November, fell ill on the 9th with left inguinal bubo and a temperature of 104°F., severe prostration, and mental stupor which soon deepened into a state of coma. Pulse weak, thready and quick. Vomiting and diarrhoea also started. He was first put on cibazol treatment with a mixture of sodium bicarbonate, stimulants, and tincture of digitalis to maintain his heart. Injections of soluseptasine and glucose were also administered every day. Vomiting and diarrhoea started on the 3rd day, when the dose of cibazol had to be reduced to one tablet every 4 hours, preceded 15 to 20 minutes by a tablet of nicotinic acid. Diarrhoea was controlled by one drachm doses of kaolin given every 2 hours. The temperature came down on the 6th day, but the patient developed complete aphasia. He however began to stammer out words after a fortnight, but resumed normal speech only after 6 weeks.

4. A Hindu male, aged 35, contracted plague on 9th December, 1944, with a bubo in the right groin. He was very toxic, restless and semi-comatose. Cibazol was started on the 1st day but on the 2nd day he developed severe vomiting. The dose of cibazol was reduced to one tablet every 4 hours, preceded by one tablet of nicotinic acid. Diarrhoea was controlled by kaolin emulsion. Fever began to come down on the 18th and the patient was soon convalescent.

(c) *Septicæmic type*—

5. A Hindu male, aged 20, unprotected, fell ill with high temperature, 105.4°F., severe prostration and unconsciousness but without any bubo. He was given cibazol, and soluseptasine and glucose by the parenteral route for toxæmia, and coramine for cardiac weakness. But all these had no effect. He developed diarrhoea the same day and succumbed within 24 hours.

(d) *Bubonic with advanced pregnancy and abortion*—

6. A female, aged 30, unprotected, fell ill with high temperature, 104°F., pulse 120, respiration 32. She had

left inguinal bubo and was 5 months pregnant. She was given cibazol. There was however no diminution in temperature. On the 5th day she had an abortion, and in spite of all efforts continued to sink and died the same day.

(e) *Bubonic with hæmorrhages*—

7. A male, aged 30, unprotected, fell ill on 13th April, 1944, with right inguinal bubo. Fever 101°F. on the 1st day. Cibazol started on the same day, but the next day temperature rose to 105°F., with marked restlessness and toxæmia. Patient had epistaxis, spitting of blood and hæmaturia. The treatment was continued and on the 4th day the temperature showed a tendency to decline. But he got diarrhoea on the 6th day, which was easily controlled by kaolin and the temperature became subnormal on the 7th day. The bubo however did not subside for another fortnight.

SULPHA DRUGS IN BACILLARY DYSENTERY

By A. N. BOSE
P. N. SEN GUPTA

and

U. P. BASU

(From Bengal Immunity Research Laboratory,
Calcutta)

It is now generally accepted that the sulphonamide drugs have a beneficial effect in bacillary dysentery. Sulphaguanidine, sulphapyridine, succinyl sulphathiazole, phthalyl sulphathiazole and sulphanilyl benzamide and even sulphanilamide are being found to be more or less beneficial in dysentery cases. But the question arises of the choice of a drug in acute infections and/or removing the persistent carriers of *B. dysenteriae*. The drug that would be able to bring about both clinical and bacteriological cure without any undesirable reaction would always be aimed at for the welfare of the persons infected as well as for the benefit of the community in which the disease is very prevalent.

Since the observations of Marshall *et al.* (1940, 1941) sulphaguanidine is being largely used in the chemotherapy of intestinal infections particularly against bacillary dysentery. But the drug has certain drawbacks. It is not cheap. Its use is often precluded by vomiting in cases which need it most (Hughes, 1944). The dosage used is usually large—an adult of average weight requiring a total dose of 50 to 55 grammes (100 to 110 tablets of 0.5 gramme each) (Clay, 1943). Brewer (1943) again noticed that in acute cases complete cure was obtained by giving as many as 180 tablets during a period of 6 days. Of course, the stool often becomes normal even with a lower dosage such as an initial dose of 12 tablets followed by a dose of 6 tablets for next 5 days (Ferriman and MacKenzie, 1944). This clinical cure may also be brought about within 3 to 4 days by using a higher total dose (116 tablets) as shown by Scadding (1944). Another drawback of sulphaguanidine is that it cannot be injected in urgent cases. Moreover, it is not so effective against *B. dysenteriae* (Sonne) (Fairbrother, 1944). Using a heroic dose of 60 tablets during first 2 days and 30

intestines and thereby exert their characteristic pharmacological action. The drug sulphanilyl benzamide again is readily absorbed from the gastro-intestinal tract (Bose and Ghosh, 1944), but it is also being found to be equally effective against dysentery in our hands. Marshall's hypothesis that the activity of a sulpha drug effective in intestinal infections is due to its poor absorption from gut, cannot be accepted as the sole explanation of the antibacterial action. The relative concentration, conjugation, rate of elimination of sulphanilamide, sulphaguanidine, sulphapyridine, sulphathiazole and sulphanilyl benzamide are recorded in table III (Frisk, 1943). Work is in progress to find out the factors on which the action of the drugs against intestinal infections depends.

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From table III it may be seen that all the drugs undergo acetylation in varying degrees. This is of much importance from the clinical point of view, as it is well known that this acetylation often lowers the activity of the parent compound, and the acetylated product being less

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Sulphanilyl benzamide ..	Rapid and complete.	5.5 to 8 within 3 hours.	Rapid; 50 to 70 per cent in 24 hours. About 90 per cent in 72 hours.	Up to 17	30 to 40

Sulphanilyl benzamide has also been found to be free from undue toxicity and is well tolerated (Bose and Ghosh, 1944). A special point is its action against *B. dysenteriae*, Sonne (Swyer and Yang, 1945). A total dosage of 12 to 15 grammes of the drug during a period of 3 to 4 days, causes a clinical cure by making the stool solid, normal in colour and free from blood or mucus. It is innocuous and at the same time clinically effective. Phthalyl sulphathiazole according to Poth

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According to the recent findings of Leishman and Kelsall (1944), 30 per cent of the tropical diseases in India are due to dysentery; out of this total, 42 per cent of the cases are of bacillary type, and about 13.8 per cent of bacillary dysentery cases are due to *Sonne* infection (*vide* table I). Therefore special measures should be adopted to eradicate this disease for the welfare of the public. It may be stressed that a bacteriological cure of bacillary dysentery is of more importance for the community, because a convalescent carrier plays a large part in disseminating the infection throughout the length and breadth of the country.

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TABLE III
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(From Frisk, 1943)

Drug	General absorption	Blood concentration mg. per cent	Elimination in urine	ACETYLATION, PER CENT	
				Blood	Urine
Sulphanilamide ..	Rapid	8 to 10 after 2 hours.	Quick and complete; 70 per cent in 24 hours.	Up to 20	50
Sulphaguanidine ..	Irregular	3 within 4 hours.	Complete within 48 hours	40	20 to 30
Sulphapyridine ..	Slow	3 to 5 within 6 hours.	Very slow 50 per cent; within 24 hours. 80 per cent within 4 days.	Up to 30	60
Sulphathiazole ..	Rapid and complete.	6 to 8 within 4 hours.	Rapid; over 80 per cent in 24 hours. About 95 per cent in 72 hours.	10 to 20	20 to 30
Sulphanilyl benzamide ..	Rapid and complete.	5.5 to 8 within 3 hours.	Rapid; 50 to 70 per cent in 24 hours. About 90 per cent in 72 hours.	Up to 17	30 to 40

Sulphanilyl benzamide has also been found to be free from undue toxicity and is well tolerated (Bose and Ghosh, 1944). A special point is its action against *B. dysenteriae*, Sonne (Swyer and Yang, 1945). A total dosage of 12 to 15 grammes of the drug during a period of 3 to 4 days, causes a clinical cure by making the stool solid, normal in colour and free from blood or mucus. It is innocuous and at the same time clinically effective. Phthalyl sulphathiazole according to Poth

soluble, brings forth undesirable side reactions. The solubility of sulphaguanidine, acetyl sulphaguanidine, sulphapyridine, and acetyl sulphapyridine does not appreciably increase with alkalinity of the solution. Sulphanilyl benzamide itself is very soluble, varying from 80 to 90 mg. per 100 c.cm. of urine at pH 6 to more than 450 mg. at pH 7.8. This compound undergoes acetylation to an extent of 30 to 40 per cent in urine, but this acetylated derivative is also readily soluble in alkaline pH.

TABLE IV
Animal used : Mice

Drug	Mode of administration	Dose mg./gm.	Mortality per cent
Sulphanilamide (sodium salt) ¹	Subcutaneous	2.79	50
Sulphaguanidine ²	Intraperitoneal	1.0	100
Sulphapyridine (sodium salt) ¹	Subcutaneous	0.93	50
Sulphathiazole (sodium salt) ¹	"	1.67	50
Phthalyl sulphathiazole ³	Intraperitoneal	0.9	50
Sulphanilyl benzamide ⁴	"	2.0	10
Sulphanilyl benzamide (sodium salt) ⁴	Intravenous	1.5	20

(¹) Frisk (1943); (²) Marshall *et al.* (1940); (³) Pick *et al.* (1944); (⁴) Bose and Ghosh (1944).

tablets for the next 2 days, Osborn and Jones (1944) noticed the efficacy of the drug in Sonne dysentery; but it exerted a constipating effect subsequently.

According to the recent findings of Leishman and Kelsall (1944), 30 per cent of the tropical diseases in India are due to dysentery; out of this total, 42 per cent of the cases are of bacillary type, and about 13.8 per cent of bacillary dysentery cases are due to Sonne infection (*vide* table I). Therefore special measures should be adopted to eradicate this disease for the welfare of the public. It may be stressed that a bacteriological cure of bacillary dysentery is of more importance for the community, because a convalescent carrier plays a large part in disseminating the infection throughout the length and breadth of the country.

TABLE I

(From Leishman and Kelsall, 1944)

Dysentery organisms	Per cent
Flexner	52.4
Shiga	15.7
Sonne	13.8
Schmitz	8.8
Boyd	8.8
Newcastle	0.5

Sulphapyridine is also a potent drug, but its defects are its liability to cause nausea, vomiting and serious renal disorders. In a dehydrating disease like dysentery, the danger is real. Another useful drug has been found in succinyl sulphathiazole (Poth and Knotts, 1942; Poth *et al.*, 1942; Hardy *et al.*, 1943).

then 0.02 gramme per 4 kilogram at 4-hour intervals until the clinical improvement is noticed. It is well tolerated (Poth and Ross, 1944) and is twice as effective as the former one—succinyl sulphathiazole. Regarding these acyl sulphathiazole drugs it may be recorded here that they may exhibit individual bacteriostatic properties but their activity is partly dependent on the breakdown of the products to sulphathiazole, or, at least to some compound containing a diazotizable amino grouping in the system. Sulphathiazole, the parent compound, is the most effective drug against various dysentery organisms *in vitro*. Table II shows that in *in vitro* experiments this drug is many times more potent against all the various dysentery organisms in a papain digest glucose-phosphate broth at pH about 7.6.

From table II it would be found that sulphathiazole is the best bacteriostatic agent against all the dysentery organisms tested. Sulphapyridine and sulphanilyl benzamide are of the same order. Phthalyl sulphathiazole is inferior to the above three compounds but is superior to sulphaguanidine particularly against Sonne, Schmitz, Boyd and Newcastle organisms. Succinyl sulphathiazole and sulphanilamide are the least effective bacteriostatic substances *in vitro*. Sulphaguanidine, the most commonly used drug, is particularly less efficacious against *B. dysenteriae* (Sonne). Sulphathiazole is, however, not being found to exert its characteristic antibacterial action in clinical application. Of course, this drug is readily absorbed from the upper alimentary tract and therefore according to the hypothesis of Marshall that the action of

TABLE II

Figures indicate concentration of the drug in mg. per 100 c.cm. broth

Drug	ORGANISMS					
	Flexner	Shiga	Sonne	Schmitz	Boyd	Newcastle
Sulphanilamide	100	Less than 100	100	100	100	100
Sulphathiazole	2	2	2	2	1	1
Succinyl sulphathiazole	100	100	100	100	50	50
Phthalyl sulphathiazole	20	20	20	20	10	10
Sulphapyridine	10	10	10	10	5	5
Sulphaguanidine	20	20	100	50	20	20
Sulphanilyl benzamide	10	10	10	10	5	5

The dosage used in clinical application is about 44 grammes or 88 tablets. It is also not so effective against Sonne dysentery (*cf.* Fairbrother, 1944; Swyer and Yang, 1945).

Phthalyl sulphathiazole is another acyl derivative of sulphathiazole whose toxicity is particularly low and which has proved to be highly specific in the treatment of Flexner bacillary dysentery (Poth, 1943). The dose would be 0.04 gramme of the drug per kilogram of body-weight every 4 hours for 12 doses and

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The liver was not palpable in any but the spleen was palpable in one.

The stools were pale, copious and porridge-like in consistency, passed daily in 18 cases and occasionally in 5. The percentage of total, split and neutral fats varied from 38.21 to 71.5 (average 46.5), 25.5 to 59.5 (average 37.5) and 3.6 to 14.9 (average 8.5) respectively. Undigested starch was present in fair quantity during the acute exacerbation of the symptoms in 2 and in traces in a few.

Blood was examined in 21 cases only. The total red cells in millions per c.mm. varied from 4 to 5 in 13, 3 to 4 in 5 and 2 to 3 in 3.

The hæmoglobin percentage (100 per cent = 14.5 grammes) was 100.0 in 8, 80 to 99 in 8, 60 to 79 in 3 and 47 to 59 in 2. Seven showed malaria parasites in their blood films, and three had attacks of fever with rigor and were treated as clinical malaria. Five cases with hæmoglobin below 80 per cent showed a dimorphic type of anæmia rather than a macrocytic anæmia. Two of them showed malaria parasites, the third was treated as clinical malaria, and the fourth had history of fever in 1942 and 1943. No record is available of the fifth.

A fractional test meal was done in 9 cases. There was achlorhydria in 5 and hypoacidity in 4.

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2. *Drug treatment.*—(a) Dilute hydrochloric acid $\frac{1}{2}$ dr. mixed with 4 oz. of water half an hour before meals.

(b) Nicotinic acid 100 to 400 mg. daily by mouth for a period varying from 7 to 20 days was found useless whether tried on admission or after the sulpha group of drugs had failed to give lasting relief.

(c) Sulphaguanidine 56 grammes and sulphadiazine or sulphapyridine 22 grammes in 6 to 7 days always controlled the diarrhoea but it recurred within a few days of the stoppage of the drugs except when the case had been in hospital for three or more weeks and had improved in general condition. A second course of the drug

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Post-mortem examination was done in 2. The heart was small in size and the muscle discoloured. The intestines showed generalized atrophy. Histopathology was studied in one, and showed degenerative changes of the myocardium and atrophy of the musculature of the intestines with fibrosis in the sub-epithelial and sub-mucous tissue.

Comment.—The disease started as dysentery or diarrhoea in the forward areas 1 to 5 months before the men went home on leave. They did not report sick either because of conditions prevailing there or through negligence. Restriction of diet, which was partly due to the food situation and partly self-imposed, added to the drain on the body tissues brought about by diarrhoea or dysentery. The syndrome described above resulted from the vicious circle thus set up.

Howat (1944) suggested that fatty diarrhoea might be a result of the frequent use of sulpha drugs in the treatment of chronic and relapsing bacillary dysentery. Nineteen of the patients in this series stated that the disease started as dysentery; 9 of them had cellular exudate in the stools. No evidence of amœbic or helminthic infection was detected except strongyloid infection in two of the fatal cases. It is very probable that majority of these cases started as bacillary dysentery. No definite information was available about any previous treatment of these patients with sulphaguanidine. There was a distinct improvement in their condition within 48 hours of putting these patients on sulpha drugs. Sulphaguanidine was used in 5 cases, 22 to 43 days after admission. Though the frequency of motions decreased, the diarrhoea with the other symptoms described above recurred occasionally in acute exacerbations. These cases were discharged as fit for duty a few days after another course of the drug. Seven cases were put on a sulpha drug after they had been on nicotinic acid 100 to 800 mg. daily for 7 to 22 days without effect. The former relieved them of the symptoms. It is improbable that one drug would cause as well

Conclusion

Amongst the various sulphonamide drugs that are now being used against bacillary dysentery phthalyl sulphathiazole and succinyl sulphathiazole are considered to be more potent. Both are well tolerated, but the latter seems to be less toxic than the former.

Sulphanilyl benzamide appears to be the least toxic and to be equally effective against various types of bacillary dysentery (specially Sonne infections). It may become the drug of choice in the treatment of dysentery cases.

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FATTY DIARRHŒA

A REPORT ON 26 CASES

By BALBIR SINGH

MAJOR, I.A.M.C.

THESE patients were admitted to a malnutrition ward of an Indian military hospital. Twenty-three of them were relieved of their symptoms; three died.

All the 23 patients except one were Muslims and non-vegetarians. They had stayed in the forward areas for a period varying from 4 to 36 months when the symptoms commenced. The majority developed diarrhœa within the first year of their stay. Seven gave a history of

being cut off by the enemy, during which period diarrhœa or dysentery first made its appearance. The diarrhœa lasted from 1 to 5 months but they did not seek admission to hospital and subsequently went on leave. Their condition became worse during their stay at home which varied from 10 days to 2½ months. On admission they had the following complaints:—

1. Frequency of motions varying from 3 to 13 in 24 hours, occasionally with mucus.
2. Distension of the abdomen after meals, and gurgling sounds.
3. Vomiting and retching after meals in 9 cases.
4. Gripping with motions.
5. Weakness.
6. Wasting.
7. 'Feverishness' in 4 cases.

According to the severity, the cases can be grouped as follows:—

(1) *Severe*.—Very weak, unable to move out of bed, mentally sluggish and apathetic; skin dry and inelastic; nose and cheeks pigmented; wasting of muscles especially of chest and face. Pinguecula with or without muddy brown pigmentation; tongue pale and papillæ atrophied, epithelium of the tip eroded; lower segment of abdomen distended after meals; spleen and liver not palpable. Respiratory and circulatory systems showed no abnormality except that the pulse was slightly rapid in some cases. Number of motions, 6 to 12 in 24 hours; stools pale, copious, porridge-like in consistency and slightly frothy; no ova, cysts, amœba or exudate on microscopic examinations; total fats in stools 50.0 per cent, split fats 40.0 per cent and neutral fats 10.0 per cent. The red cell count varied from 4 to 5 millions and the hæmoglobin 80 to 100 per cent. The leucocyte count was slightly below normal. Some cases had hypochlorhydria and others achlorhydria. It could not be ascertained whether the achlorhydria was histamine-fast or not, as histamine was not available.

(2) *Moderately severe*.—Physical condition was not so bad, and the prostration was much less; no mental symptoms. Other features were the same as in severe cases.

(3) *Mild*.—Very little or no emaciation; characteristic stools passed daily or occasionally; number of motions averaged 3 to 6 in 24 hours; recovered without any drug treatment.

Clinical details.—Emaciation was marked in 14 and slight in 9 cases. The skin was dry in 7. The nose and cheeks were pigmented in 8. The scrotum showed scaly dermatitis in one and patches of old scabies lesions in another. There was thickening of the skin of the scrotum and penis with flat-topped follicles in one, and scaly dermatitis in one. None of them showed vascularization of the cornea. Thirteen had pre-ptygium or pinguecula. The conjunctiva was muddy-coloured, and showed brownish pigmentation in 3 and degenerative patches in 3. Two had scleritis. The character of the tongue was

recorded in 21. It was pale in 10, raw and red in 4, smooth in 11, fissured in 2, eroded at the edges and tip in 6 and at the tip only in another 6 cases. Two had ulcers on the frenum linguae. All of them complained of soreness of the tongue at times during their stay in hospital or before admission, and of difficulty in swallowing very lightly spiced food. Three of them complained of irritation even after taking grape juice or water. There were indentations of the teeth on the edges of the tongue in 3. Two had angular stomatitis.

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being cut off by the enemy, during which period diarrhoea or dysentery first made its appearance. The diarrhoea lasted from 1 to 5 months but they did not seek admission to hospital and subsequently went on leave. Their condition became worse during their stay at home which varied from 10 days to 2½ months. On admission they had the following complaints:—

1. Frequency of motions varying from 3 to 13 in 24 hours, occasionally with mucus.
2. Distension of the abdomen after meals, and gurgling sounds.
3. Vomiting and retching after meals in 9 cases.
4. Gripping with motions.
5. Weakness.
6. Wasting.
7. 'Feverishness' in 4 cases.

According to the severity, the cases can be grouped as follows:—

(1) *Severe*.—Very weak, unable to move out of bed, mentally sluggish and apathetic; skin dry and inelastic; nose and cheeks pigmented; wasting of muscles especially of chest and face. Pinguecula with or without muddy brown pigmentation; tongue pale and papillae atrophied, epithelium of the tip eroded; lower segment of abdomen distended after meals; spleen and liver not palpable. Respiratory and circulatory systems showed no abnormality except that the pulse was slightly rapid in some cases. Number of motions, 6 to 12 in 24 hours; stools pale, copious, porridge-like in consistency and slightly frothy; no ova, cysts, amœba or exudate on microscopic examinations; total fats in stools 50.0 per cent, split fats 40.0 per cent and neutral fats 10.0 per cent. The red cell count varied from 4 to 5 millions and the hæmoglobin 80 to 100 per cent. The leucocyte count was slightly below normal. Some cases had hypochlorhydria and others achlorhydria. It could not be ascertained whether the achlorhydria was histamine-fast or not, as histamine was not available.

(2) *Moderately severe*.—Physical condition was not so bad, and the prostration was much less; no mental symptoms. Other features were the same as in severe cases.

(3) *Mild*.—Very little or no emaciation; characteristic stools passed daily or occasionally; number of motions averaged 3 to 6 in 24 hours; recovered without any drug treatment.

Clinical details.—Emaciation was marked in 14 and slight in 9 cases. The skin was dry in 7. The nose and cheeks were pigmented in 8. The scrotum showed scaly dermatitis in one and patches of old scabies lesions in another. There was thickening of the skin of the scrotum and penis with flat-topped follicles in one, and scaly dermatitis in one. None of them showed vascularization of the cornea. Thirteen had pre-ptyerygium or pinguecula. The conjunctiva was muddy-coloured, and showed brownish pigmentation in 3 and degenerative patches in 3. Two had scleritis. The character of the tongue was

recorded in 21. It was pale in 10, raw and red in 4, smooth in 11, fissured in 2, eroded at the edges and tip in 6 and at the tip only in another 6 cases. Two had ulcers on the frenum linguae. All of them complained of soreness of the tongue at times during their stay in hospital or before admission, and of difficulty in swallowing very lightly spiced food. Three of them complained of irritation even after taking grape juice or water. There were indentations of the teeth on the edges of the tongue in 3. Two had angular stomatitis.

The liver was not palpable in any but the spleen was palpable in one.

The stools were pale, copious and porridge-like in consistency, passed daily in 18 cases and occasionally in 5. The percentage of total, split and neutral fats varied from 38.21 to 71.5 (average 46.5), 25.5 to 59.5 (average 37.5) and 3.6 to 14.9 (average 8.5) respectively. Undigested starch was present in fair quantity during the acute exacerbation of the symptoms in 2 and in traces in a few.

Blood was examined in 21 cases only. The total red cells in millions per c.mm. varied from 4 to 5 in 13, 3 to 4 in 5 and 2 to 3 in 3.

The hæmoglobin percentage (100 per cent = 14.5 grammes) was 100.0 in 8, 80 to 99 in 8, 60 to 79 in 3 and 47 to 59 in 2. Seven showed malaria parasites in their blood films, and three had attacks of fever with rigor and were treated as clinical malaria. Five cases with hæmoglobin below 80 per cent showed a dimorphic type of anæmia rather than a macrocytic anæmia. Two of them showed malaria parasites, the third was treated as clinical malaria, and the fourth had history of fever in 1942 and 1943. No record is available of the fifth.

A fractional test meal was done in 9 cases. There was achlorhydria in 5 and hypoacidity in 4.

1. *Treatment.*—Diet. All cases were put on milk, curd, fresh fruit juice, liver juice, marmite, raw eggs, bread and butter. The feeds were given every two hours starting with 2 oz. or less especially in those cases that complained of vomiting and retching. Diets were gradually increased and built up to solids after a week. Bread and butter were withheld when the diarrhoea did not stop, or recurrence took place.

2. *Drug treatment.*—(a) Dilute hydrochloric acid $\frac{1}{2}$ dr. mixed with 4 oz. of water half an hour before meals.

(b) Nicotinic acid 100 to 400 mg. daily by mouth for a period varying from 7 to 20 days was found useless whether tried on admission or after the sulpha group of drugs had failed to give lasting relief.

(c) Sulphaguanidine 56 grammes and sulphadiazine or sulphapyridine 22 grammes in 6 to 7 days always controlled the diarrhoea but it recurred within a few days of the stoppage of the drugs except when the case had been in hospital for three or more weeks and had improved in general condition. A second course of the drug

controlled the diarrhoea. These cases were discharged as relieved of the symptoms a week or two after the second course and no follow-up was possible after this.

3. *Blood transfusion.*—Six cases were each given 8 oz. of fresh whole blood twice at a week's interval. There was no change in their conditions after the transfusions.

Three fatal cases.—These patients were more emaciated and prostrated on admission than those who recovered. They were mentally dull and confused. The spleen was 'three fingers' in one and just palpable in another. Stools were pale, copious and, except in one, fluid or porridge-like in consistency. Cellular exudate in 2 and larvæ of strongyloides also in 2. These patients died after 7 days, 14 days and two months' stay in hospital.

Post-mortem examination was done in 2. The heart was small in size and the muscle discoloured. The intestines showed generalized atrophy. Histopathology was studied in one, and showed degenerative changes of the myocardium and atrophy of the musculature of the intestines with fibrosis in the sub-epithelial and sub-mucous tissue.

Comment.—The disease started as dysentery or diarrhoea in the forward areas 1 to 5 months before the men went home on leave. They did not report sick either because of conditions prevailing there or through negligence. Restriction of diet, which was partly due to the food situation and partly self-imposed, added to the drain on the body tissues brought about by diarrhoea or dysentery. The syndrome described above resulted from the vicious circle thus set up.

Howat (1944) suggested that fatty diarrhoea might be a result of the frequent use of sulpha drugs in the treatment of chronic and relapsing bacillary dysentery. Nineteen of the patients in this series stated that the disease started as dysentery; 9 of them had cellular exudate in the stools. No evidence of amœbic or helminthic infection was detected except strongyloid infection in two of the fatal cases. It is very probable that majority of these cases started as bacillary dysentery. No definite information was available about any previous treatment of these patients with sulphaguanidine. There was a distinct improvement in their condition within 48 hours of putting these patients on sulpha drugs. Sulphaguanidine was used in 5 cases, 22 to 43 days after admission. Though the frequency of motions decreased, the diarrhoea with the other symptoms described above recurred occasionally in acute exacerbations. These cases were discharged as fit for duty a few days after another course of the drug. Seven cases were put on a sulpha drug after they had been on nicotinic acid 100 to 800 mg. daily for 7 to 22 days without effect. The former relieved them of the symptoms. It is improbable that one drug would cause as well

Conclusion

Amongst the various sulphonamide drugs that are now being used against bacillary dysentery phthalyl sulphathiazole and succinyl sulphathiazole are considered to be more potent. Both are well tolerated, but the latter seems to be less toxic than the former.

Sulphanil benzamide appears to be the least toxic and to be equally effective against various types of bacillary dysentery (specially Sonne infections). It may become the drug of choice in the treatment of dysentery cases.

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as relieve the same condition. If sulpha drugs are prone to give rise to sprue-like symptoms, these cases should have become worse after their administration.

Acknowledgment

This opportunity is taken to thank Lieut.-Colonel A. Y. D. Dhabalkar, I.A.M.C., for his encouragement and personal interest in the investigation of these cases.

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[The syndrome described in this paper closely resembles the condition of 'para-sprue' in which the value of sulpha drugs has already been reported.—
EDITOR, I.M.G.]

VIABILITY OF DYSENTERY, ENTERIC AND CHOLERA ORGANISMS IN MILK CURD (DAHI)*†

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IN Calcutta, large quantities of milk curd (*dahi*) are consumed as food especially in feasts. It is prepared by vendors in open earthen pots, and sometimes kept for two or more days before it is consumed; there is the possibility of its being contaminated with dysentery, enteric and cholera organisms.

Twenty-seven samples of curd, 16 'sweet' and 11 'sour', were bought from different shops in Calcutta for testing. Smears showed lacto-bacilli in all of them. Their pH, determined by colorimeter method, ranged from 4.2 to 4.7.

Viability tests

Four drops of the culture of the above three organisms were separately added to about 10 c.cm. of curd before and after neutralization

*The paper was read before the Indian Science Congress Association held at Nagpur in January 1945.
†Rearranged by Editor.

with caustic soda at room temperature, and subcultures were made every 5, 10, 15, 30 and 60 minutes and 2, 3 and 20 hours.

(1) Viability of *V. cholera*, *Inaba* and *Ogawa* subtypes mixed

Nine samples were tested with this mixture and the results obtained with four specimens are given in the table. The results were the same in other samples.

It will be seen from the table that cholera vibrios are completely killed within 5 minutes by sweet as well as sour *dahi*. After neutralization of the curd, when the pH becomes about 7.2, its killing power is lost.

(2) Viability of *Bact. typhosum*

All the 27 samples were tested with this organism and the results are given in the following table :—

Curd number	Nature	Growth of subculture made in				
		5 min.	10 min.	15 min.	30 min.	60 min.
1	Sweet	+	+	+	+	—
2	"	+	..	+	—	—
3	"	+	..	+	—	—
4	"	..	—	—	—	—
5	"	..	—	—	—	—
7	"	—	—	—
8	"	—	—	—
10	"	+	+	—
11	"	+	+	—
12	"	+	+	—
16	"	+	—	—	—	—
17	"	—	—	—	—	—
18	"	+	+	+	+	—
22	"	—	—	—
23	"	—	—	—
24	"	+	—	—
6	Sour	..	—	—	—	—
9	"	—	—	—
13	"	+	—	—
14	"	+	+	—
15	"	+	+	—
19	"	—	—	—	—	—
20	"	—	—	—	—	—
21	"	+	—	—	—	—
25	"	—	—	—
26	"	—	—	—
27	"	—	—	—

Dahi No.	Nature	pH	Growth of subculture made in						
			5 min.	15 min.	30 min.	60 min.	2 hrs.	4 hrs.	20 hrs.
1	Sweet {	(Non-neutralized) 4.4	—	—	—	—	—	—	—
		(Neutralized) .. 7.0	+	+	+	+	+	—	—
2	Sour {	(Non-neutralized) 4.4	—	—	—	—	—	—	—
		(Neutralized) .. 7.2	+	+	+	+	+	—	—
6	Sour {	(Non-neutralized) 4.2	—	—	—	—	—	—	—
		(Neutralized) .. 7.2	+	+	+	+	+	+	+
9	Sour {	(Non-neutralized) 4.4	—	—	—	—	—	—	—
		(Neutralized) .. 7.1	+	+	+	+	—	—	—

+ means growth positive; — means no growth, i.e. not viable.

This table shows that in all the 27 samples, typhoid bacilli were killed in one hour; in the majority of samples (20) within 30 minutes, in 16 within 15 minutes and in a few within 5 to 10 minutes.

After neutralization, no bactericidal effect on the typhoid bacilli was seen even up to 3 hours, but the effect was seen after 20 hours when the pH came back near the original level.

(3) Viability of a mixture of *Bact. flexneri* and *Bact. shigæ*

Twenty-one samples of curd were tested with this mixture and the results are given in the following table :—

Curd number	Growth in subculture made in					
	15 min.	30 min.	60 min.	2 hrs.	4 hrs.	20 hrs.
7	+	—	—	—	..	—
8	+	+	—	—	..	—
10	+	—	—	—	..	—
11	+	+	—	—	..	—
12	+	+	—	—	..	—
16	+++	++	++	+	—	—
17	+++	++	+	—	..	—
18	+++	+++	++	++	—	—
22	..	++	++	++	—	—
23	..	+++	++	—	—	—
24	..	+++	++	—	—	—
9	+	+	—	—	..	—
13	+	+	—	—	..	—
14	+	+	—	—	..	—
15	+	+	—	—	..	—
19	+++	+++	+++	—	..	—
20	+++	+++	+	—	..	—
21	+++	+++	++	—	..	—
25	..	++	—	—	—	—
26	..	+	—	—	—	—
27	..	+	—	—	—	—

No bactericidal effect was seen when the curd was neutralized with caustic soda solution.

It will be seen from the above table that in all the 21 samples the dysentery bacilli were killed

within 4 hours and 20 hours; in the majority (17) within 2 hours, in 12 within an hour, and in 2 within half an hour, and none within 15 minutes.

(4) Comparative bactericidal effect of lactic and other acids, adjusted to pH 4.4

Sterile mixtures of acids were made in 1 per cent peptone water and the pH was adjusted to 4.4, i.e. approximately the pH of natural curd. Peptone was used for providing food to the organisms. It was found that uninoculated mixtures retained the same pH after 24 hours. To 5 c.cm. quantities of the mixtures, 20 drops of young broth culture of organisms were added and then put at 37°C. in the incubator. The results are given in the table.

If the inoculum consisted of 10 drops only of the cultures, then acetic acid exerted a complete bactericidal effect in 30 minutes. The above acids do not kill pure cultures of lacto-bacilli in 24 hours.

It will be seen from the table that—

1. Hydrochloric, acetic and citric acids in comparison with lactic acid have a poor bactericidal effect on *Bact. flexneri* and *Bact. typhosum*.
2. There is not much difference between pure lactic acid solution and natural whey containing lactic acid and other products in the above bactericidal effect.
3. All the above acids are highly and quickly bactericidal to *V. cholera* excepting citric acid which takes a longer time to kill.

As citric acid was found poorly bactericidal to cholera vibrios, and since lime juice is frequently used with food as a prophylactic for cholera during an epidemic, it was decided to try the effect of fresh lime juice on *V. cholera*.

It will be seen that diluted fresh lime juice, pH 4.4, does not exert any bactericidal effect on *Bact. flexneri* and *Bact. typhosum* in 24 hours, but does so on *V. cholera* in half an hour. Undiluted juice kills vibrios within 5 minutes.

Organisms	pH	Hydrochloric acid	Acetic acid	Citric acid	Lactic acid	Dahi-whey containing live pure lacto-bacilli 4.5
		4.4	4.4	4.4	4.4	
Time in hours	..	½ 1 2 4 24	½ 1 2 4 24	½ 1 2 4 24	½ 1 2 4 24	½ 1 2 4 24
<i>Bact. flexneri</i>	{ Growth Turbidity	+ + + + + - - - - ±	+ + + + + - - - - -	+ + + + + - - - - +	+ - - - - - - - - -	- - - - - Difficult to ascertain.
<i>Bact. typhosum</i>	{ Growth Turbidity	+ + + + + - - - - -	+ + + - - - - - - ±	+ + + + + - - - - + +	- - - - - - - - - -	- - - - -
Time in minutes	..	1 2 5 30 ..	1 2 5 30 ..	1 2 5 30 ..	1 2 5 30 ..	1 2 5 30 ..
<i>V. cholerae</i> (Inaba)	{ Growth Turbidity	- - - - .. - - - - ..	- - - - .. - - - - ..	+ + + - .. - - - - ..	- - - - .. - - - - ..	- - - -

		Lime juice fresh, pH adjusted to 4.4 in 1 per cent peptone water					Lime juice pure, pH 2.8				
		$\frac{1}{2}$	1	2	4	24					
Time in hours	..										
<i>Bact. flexneri</i>	..	+	+	+	+	+					
<i>Bact. typhosum</i>	..	+	+	+	+	+					
Time in minutes	..	5	10	20	30	60	5	10	20	30	60
<i>V. cholerae</i> , Inaba subtype		++	+	+	—	—	—	—	—	—	—
<i>V. cholerae</i> , Ogawa subtype		+++	+	+	—	—	—	—	—	—	—

(5) Bactericidal effect of lacto-bacilli

The results of the plating of equal quantities of lacto-bacilli and *Bact. flexneri* on agar and glucose agar, immediately, 30 minutes after and 1 day after, are given in the following table:—

		<i>Bact. flexneri</i>	Lacto-bacillus
Immediately	Agar ..	+++	+
	Glucose agar	++	+
30 minutes after	Agar ..	+++	+
	Glucose agar	+++	+
One day after	Agar ..	+++	—
	Glucose broth	—	+

(A medium made with killed and washed lacto-bacilli does not inhibit dysentery bacilli.)

On plate cultures, colonies of *Bact. flexneri* and lacto-bacilli grow side by side. There is no inhibition of the former by the latter. Thirty minutes' contact with lacto-bacilli does not kill *Bact. flexneri* in nutrient broth. In one day's contact lacto-bacilli are overgrown by *Bact. flexneri*, but in glucose broth *Bact. flexneri* are killed. This was found due to lowered pH (6.5) in glucose broth.

Summary

Cholera vibrios are completely killed within 5 minutes by sweet as well as sour milk-curds (*dahi*). Typhoid bacilli are destroyed completely in one hour; in 20 out of 27 samples in 30 minutes, in 16 in 15 minutes and in a few within 5 to 10 minutes. Dysentery bacilli are most resistant but these are killed in 4 hours; in 17 out of 21 samples within 2 hours, in 12 within an hour but none within 15 minutes. Sweet and sour curds both behave in the same way with all these organisms, and lactic acid is the chief bactericidal agent.

Hydrochloric, acetic and citric acids possess poor bactericidal action on the dysentery and typhoid bacilli in comparison with lactic acid; they are highly and quickly bactericidal to

V. cholerae excepting citric acid which takes a longer time. Diluted fresh lime juice, pH 4.4, kills cholera vibrios in half an hour and undiluted lime juice within five minutes; it does not exert any bactericidal effect on *Bact. flexneri* or *Bact. typhosum*.

PULMONARY EOSINOPHILOSIS

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TERMS like 'pseudo-tuberculosis with high eosinophilia', 'benign eosinophile leukæmia', 'tropical eosinophilia' and 'eosinophilic lung' have been used by different writers to describe the same clinical syndrome with more or less the same symptomatology. A few cases with massive eosinophilia, cough, breathlessness, bronchial spasms and disseminated shadows in the radiograph were independently seen by the writer in the chest department of King George Hospital, Vizagapatam, and a note about the same was published in the annual report of the hospital 6 years ago. The object of this paper is to give a brief review of cases seen during 14 months in an Indian General Hospital, along with a few new observations on symptomatology and the results of the cold agglutination reaction.

Incidence and ætiology.—Out of 946 cases admitted for respiratory troubles, 85 were diagnosed as pulmonary eosinophilosis.

Age.—Age distribution cannot be judged from the figures given in this review, as admissions to a military hospital are confined to male adults. The majority in this series were between the ages of 20 and 30. Twenty-four were between 20 and 25, 41 between 25 and 30, and the remaining above 30.

Province.—Weingarten (1943) reported that all his cases had lived near the sea for a long time before developing symptoms. In the present series, 34 originally belonged to Madras, 16 to Punjab, 15 to United Provinces, 8 to Bombay and 12 to Bengal. All of them had however served in different parts of East

Bengal or Assam for over 3 months before reporting sick. It is thus not the influence of the sea so much as that of a humid climate, that seems to have an ætiological relationship to pulmonary eosinophilosis.

Signs and symptoms: Chronic type.—Seventy-seven cases belonged to this group. Cough was the main symptom in all. It was associated with intermittent fever in 51 cases. The onset was invariably insidious.

The duration was over three months. Those who gave over six months' history have had remissions and intermissions.

In many of the cases, cough was not productive but very disturbing. Paroxysms of cough, of dry harsh and explosive character used to occur often during night. Bronchial spasm frequently accompanied the paroxysm. Typical asthmatic attacks were complained of in 20 cases. Expectoration when present was thick, viscid and mucoid. Only six cases had copious sputum. Seventy-two cases had breathlessness on exertion as one of the main symptoms. All the cases in this group were afebrile at the time of admission to hospital. In nine patients, however, cough had developed for the first time during a previous malarial attack.

Acute type.—Eight cases come under this category. The onset was sudden with high fever and cough. Two had been treated as clinical malaria. In three, parasites were actually found. The remaining three had been treated as broncho-pneumonia previously. All these cases were running a temperature varying from 99 to 102 when admitted to this hospital. In four cases, malaria was definitely co-existing at the time of admission. Cough, breathlessness, bronchial spasm, and extreme lassitude were the chief symptoms in these cases. Expectoration was very scanty. The course apparently seemed to be self-limiting as the symptoms cleared up within 2 to 4 weeks after admission without any specific treatment. Only in two cases of this type was one injection of N.A.B. given.

Physical signs were few in both the groups. When bronchial spasm was present, rhonchi could be heard. Otherwise a few sticky râles more marked at the bases were all that could be detected in the majority of cases. Long-standing cases with asthmatic attacks and copious expectoration showed hyper-resonance suggestive of emphysema and coarse râles. Slight tachycardia was a constant finding. The pulse rate varied from 80 to 100. Enlargement of the spleen was not present as a rule except in those with previous history of malaria.

Investigations.—Blood showed absolute eosinophilosis. Eosinophile percentages varied from 15 to 80. Total W.B.C. count gave invariably high figures ranging from 10 to 50 thousand. Six cases in which bone marrow examination by sternal puncture was done showed the same high eosinophilia. Clumps of eosinophiles could be

seen in the sputum as well. No immature cells were seen in the blood.

Radiological appearances were essentially the same as those described by Weingarten. Disseminated shadows each of the size of a split pea occurring equally in both lung fields was the constant finding. I agree with him that the distribution of the shadows suggest a bronchogenic dissemination. I had however two cases in which the shadows were distributed so uniformly as to suggest a hæmatological spread simulating miliary tuberculosis.

Cold agglutination.—Turner et al. (1943) reported on cold agglutination in atypical pneumonia; this induced the writer to test the sera of patients suffering from pulmonary eosinophilosis for the same reaction. It was a surprise to find consistently high titre values. The results in the first 61 cases have already been published in the *Lancet* (Viswanathan and Natarajan, 1945).

Unusual features.—Two patients had generalized enlargement of lymphatic glands along with pulmonary symptoms. There was no history of syphilis nor was the Wassermann positive. Pleurisy with effusion occurred in another patient while he was under investigation. Eosinophiles in large numbers were found in the pleural fluid. Hæmoptysis was present in three cases. Four patients complained of palpitation and precordial pain on the basis of which a provisional diagnosis of effort syndrome had been made. All these atypical symptoms disappeared during the course of treatment.

Diagnosis.—A history of cough with or without fever, breathlessness on exertion and/or asthmatic attacks, an eosinophile count of over 20 per cent coupled with a high white cell count, and the radiographic appearance of diffuse mottling in the lungs, are the data on which a diagnosis of pulmonary eosinophilosis is made. As the characteristic x-ray findings are seen only during the active phase, a negative x-ray does not rule out the diagnosis.

After even the first injection of arsenicals the eosinophile count shows a sharp rise. In a few cases the count was less than 20 per cent. In them an initial marked rise in the eosinophiles after an injection of N.A.B. was taken as diagnostic evidence. Eosinophile and total counts done in 15 cases of syphilis before and after injections of N.A.B. showed no appreciable alteration. We had a few doubtful cases with eosinophiles varying from 10 to 20 per cent and white cell counts from 9,000 to 14,000. The very first injection of N.A.B. brought the counts nearly to normal; but the signs and symptoms of bronchitis still persisted. The diagnosis of eosinophilosis therefore was not made in those cases. In true eosinophilosis on the other hand the initial sharp rise in the counts persisted for some days after the treatment was started, but there was marked and early amelioration of the symptoms. All other

any of the categories. A high absolute eosinophilia, which persists as long as the symptoms last, is not seen in any other condition. The presence of increased eosinophiles not only in the peripheral blood but also in the bone marrow, the finding of clumps of eosinophile cells in the sputum, the frequency of bronchial spasms, and paroxysmal cough, suggest very strongly a general body response. The nature of the factor that brings about this response is unknown. Some writers are of opinion that it is an allergic manifestation. The presence of bronchial spasms in a number of cases is in its favour. The presence however of general constitutional symptoms like fever and loss of weight, and local symptoms like cough and breathlessness and the constant finding of persistent absolute eosinophilia point towards an infective process. Carter *et al.* (1944) found mites in 17 cases out of 28 who were suffering from chronic respiratory troubles. In three cases they found leucocytosis and high eosinophilia in the blood. If only they had found eosinophilia in all the cases in which they found mites in the sputum it could have formed a satisfactory evidence for the causation of pulmonary eosinophilia. We searched for mites in six cases adopting the technique described by Carter, but our attempts were not successful. Unless and until more extensive investigation is made, one cannot pass any opinion on this interesting finding.

The high titre cold agglutination which we found in 90 per cent of the cases brings the condition in a line with atypical pneumonia. The diffuse mottled shadows seen in the x-ray are perhaps due to miliary broncho-pneumonia infiltrations. Is it possible that pulmonary eosinophilia also is a virus infection?

Name.—Paucity of accurate knowledge of the condition is the reason for multiplicity of names by which it is called even within the short period of its recognition. To the names like pseudo-tuberculosis, tropical eosinophilia, eosinophilic lung, and Weingarten's eosinophilia, the writer has ventured to add another, namely pulmonary eosinophilia. If it is to be called

Pulmonary eosinophilia

Case number	Cold agglutination, titre	Eosinophiles, per cent	Total white cell count
1	1 : 256	25	15,000
2	1 : 256	32	22,000
3	1 : 1,024	86	30,500
4	1 : 512	56	15,000
5	1 : 512	88	42,000
6	1 : 32	25	15,000
7	1 : 1,024	30	23,000
8	1 : 8	50	14,000
9	1 : 64	23	24,000
10	1 : 1,024	68	34,000
11	1 : 512	24	25,000
12	1 : 1,024	57	22,000
13	1 : 256	23	15,000

Pulmonary eosinophilia—concl.

Case number	Cold agglutination, titre	Eosinophiles, per cent	Total white cell count
14	1 : 32	25	21,000
15	Neg.	73	19,000
16	1 : 16	22	16,000
17	1 : 128	19	25,000
18	1 : 128	44	18,000
19	Neg.	25	17,000
20	1 : 1,024	62	35,000
21	1 : 512	62	45,000
22	1 : 64	22	14,000
23	1 : 16	20	15,000
24	Neg.	36	13,500
25	1 : 64	42	25,000
26	1 : 1,024	20	22,000
27	1 : 1,024	30	28,000
28	1 : 1,025	44	50,000
29	1 : 64	58	12,000
30	1 : 64	22	15,000
31	1 : 128	35	14,800
32	1 : 4	20	17,000
33	1 : 128	55	25,000
34	1 : 512	52	32,000
35	1 : 256	68	19,000
36	1 : 8	22	17,000
37	1 : 64	28	21,000
38	Neg.	60	17,000
39	1 : 64	68	32,000
40	1 : 64	30	14,000
41	1 : 64	28	23,000
42	1 : 64	25	20,000
43	1 : 128	48	32,000
44	Neg.	44	14,000
45	Neg.	54	11,000
46	1 : 64	83	56,000
47	1 : 8	30	15,000
48	1 : 16	45	17,000
49	1 : 128	27	21,000
50	1 : 2,048	69	32,000
51	Neg.	59	17,000
52	1 : 16	78	25,000
53	1 : 1,024	50	32,000
54	1 : 512	22	17,000
55	1 : 256	23	21,000
56	1 : 1,024	32	31,000
57	1 : 64	37	22,000
58	1 : 512	54	25,000
59	1 : 64	17	14,000
60	1 : 1,024	69	24,000
61	1 : 16	32	22,000
62	Not done	59	34,000
63	Not done	26	21,000
64	Not done	64	32,000
65	Not done	15	19,000
66	Not done	25	15,000
67	1 : 64	45	18,600
68	1 : 129	28	16,600
69	Neg.	21	17,300
70	1 : 512	19	81,000
71	Neg.	41	24,000
72	1 : 512	16	15,400
73	1 : 32	35	8,200
74	1 : 256	11	18,800
75	1 : 64	58	36,600
76	1 : 512	61	44,400
77	1 : 64	17	22,000
78	Neg.	13	18,000
79	1 : 128	18	14,000
80	1 : 64	17	12,000
81	1 : 1,024	16	21,000
82	1 : 512	31	14,000
83	1 : 1,024	20	11,000
84	1 : 256	14	8,500
85	1 : 2,048	64	34,000

incubate at 37°C. for half an hour; read for hæmolysis. The strongest dilution of the antigen permitting a complete hæmolysis corresponds to the anticomplementary activity short of 1 MHD of complement, and this is the dilution of the antigen to be used in the test proper.

This dilution is then tested for hæmolytic activity by incubating 0.75 c.c. of this dilution with 0.25 c.c. of sensitized cell suspension. The antigen is usually found to be non-hæmolytic.

The power of fixation of the antigen is tested by putting up comparative tests with a series of known sera using a known antigen and the new antigen.

Supposing that 1/60 is the working dilution arrived at by titration, in order to make up the dilution needed for the test proper, a total of 12 c.c. of saline will be required for the residue left after evaporation of 0.1 c.c. of the benzolic solution.

The titration of the antigen is not repeated daily, but the method of titration of the complement and the putting up of an antigen control during the test proper, serves to check the correctness of the antigen titre.

2. *Titration of the complement.*—1 : 10 dilution of the complement in normal saline is first prepared. From this 1/20, 1/30, 1/40, 1/50, . . . 1/120 dilutions are made. Two rows of tubes are set up on a rack to correspond to these dilutions of the complement. Two tubes, one behind the other, correspond to each dilution. In the tubes of the first row are placed 0.25 c.c. of the corresponding complement dilution and 0.5 c.c. of normal saline. In the tubes of the back row are put 0.25 c.c. each of the corresponding complement dilution, 1/25 dilution of inactivated negative serum, and the working dilution of the antigen. The tubes are kept at room temperature for half an hour, then incubated at 37°C. for half an hour. Then 0.25 c.c. of sensitized sheep cells is added to each tube and these are incubated at 37°C. for half an hour, after which the minimum hæmolytic dose (MHD) of the complement is read. This is taken as the highest dilution at which there is complete lysis of the sheep cells. The tubes in the two rows usually show a similar degree of lysis. If there is a disagreement in the titre as indicated in the two rows, this is usually due to the defect in the antigen dilution, and can be rectified by again titrating the antigen against 1 MHD of complement in the presence of 1/25 dilution of a negative serum, and using the antigen in the new working dilution thus obtained.

3. *The test proper.*—The serum to be tested is inactivated to destroy the complement by heating to 55°C. for half an hour in a water bath. 1 : 25 dilution is prepared by mixing 0.1 c.c. of serum with 2.4 c.c. of normal saline.

The antigen dilution is made up as described previously (*vide supra*).

Two strengths of complement dilution are made so as to contain 2 MHD and 5 MHD in a volume. Suppose 1 : 80 is the titre (MHD) of the complement, a 1 : 40 solution of the complement will contain 2 MHD and a 1 : 16 solution 5 MHD in a volume.

Three tubes, placed one behind the other, are required for testing each serum; the first tube is for serum control with 2 MHD of complement, the second and the third for the test with the antigen and 2 and 5 MHD of complement respectively.

An ensemble

Tube 1. Serum 1/25 dilution 0.25 c.c. + normal saline 0.25 c.c. + 2 MHD complement in 0.25 c.c.

Tube 2. Serum 1/25 dilution 0.25 c.c. + antigen dilution 0.25 c.c. + 2 MHD complement in 0.25 c.c.

Tube 3. Serum 1/25 dilution 0.25 c.c. + antigen dilution 0.25 c.c. + 5 MHD complement in 0.25 c.c.

Mix, leave at room temperature for half an hour, then in an incubator at 37°C. for half an hour.

Add sensitized sheep cells 0.25 c.c. to each tube, mix; incubate at 37°C. for half an hour. Read for hæmolysis.

The following general controls are put up along with the test proper :—

1. Antigen control : 0.25 c.c. of each of the following : antigen dilution, 1/25 dilution of negative serum, 1 MHD of complement.

2. Negative serum control : same as 1 but 2 MHD of complement is used.

3. Positive serum control : a known positive serum put up as in the test proper.

4. Cell suspension control : 0.25 c.c. of cell suspension put up with 0.75 c.c. of normal saline.

The method of recording the results of the test

The degree in inhibition of hæmolysis in the different tubes is read as follows :—

Complete inhibition of lysis	=	+	positive.
A trace of lysis	=	T	} doubtful.
More than a trace of lysis	=	±	
Almost complete lysis	=	? -	} negative.
Complete lysis	=	-	

A trace of lysis is detected by leaving the tube in a refrigerator overnight to allow the cells to settle down to the bottom of the tube.

The control tubes 1 and 2 should show complete lysis; the positive serum control should show no lysis with 2 and 5 MHD complement; the cell suspension tube should show no lysis.

Any serum that shows any inhibition of lysis in the serum control tube is to be regarded as anticomplementary; the other tubes are of no value; no opinion as to fixation of the complement by this serum in the presence of antigen can be given.

With complete lysis in the serum control tube, complete inhibition of lysis with 2 MHD of complement along with complete or almost complete inhibition (? T) with 5 MHD is reported as 'strongly positive'; complete inhibition of lysis with 2 MHD, with partial or no inhibition with 5 MHD, is reported as 'positive'; a trace of lysis or partial lysis with 2 MHD, with partial or no inhibition with 5 MHD, is reported as 'doubtful'; and complete or almost complete lysis with 2 MHD complement as 'negative'.

Significance

As pointed out in the previous publications on the subject of complement-fixation test for kala-azar by the writer, in the absence of severe (lepromatous) leprosy and post-kala-azar dermal leishmaniasis, a positive or strongly positive reaction with this test is indicative of kala-azar. It should be borne in mind, however, that a very small proportion of clinically obvious cases of chronic pulmonary tuberculosis gives a positive reaction. This is not a serious drawback. The doubtful reaction is regarded as an indication for further clinical and parasitological investigation. A negative reaction almost rules out kala-azar except in some very

causes of eosinophilia were excluded by thorough examination.

Examination of blood smears is a routine investigation done in all medical cases admitted to army medical units in the tropics, and in a thick drop, it is very easy to find out whether there is increase in eosinophiles or not. Sixteen cases in the series were detected during the course of routine blood examination for malaria.

Treatment.—Intravenous N.A.B. was given in all cases. After an initial dose of 0.15 gramme, 0.3 gramme was given subsequently every 5 days. The injections were stopped when the symptoms completely disappeared. A complete course consisted of eight injections. It was found necessary to repeat the course of treatment in three cases before they became symptom free.

Oral administration of carbarsone was tried in two cases without success. The one case in which penicillin was tried did not respond. Subsequent arsenic injections cleared up the symptoms in all the three. Adrenalin injections controlled bronchial spasms when present. But they seemed to have no influence either on the blood picture or on any of the other symptoms. In one of the acute cases however the condition cleared up remarkably after a few adrenalin injections given to control bronchial spasm. Perhaps the symptoms would have cleared up in any case, as the acute type appeared to be rapidly self-limiting.

Prognosis.—Cases seen by the writer in civil practice and those reported by Frimodt-Møller took several months to recover as they were not treated on any special lines. With arsenical injections, however, the improvement is rapid and certain. Three cases relapsed. One had treatment for the same trouble in one of the hospitals in Poona. He and one of the remaining who was admitted to this hospital after two months were cured by further courses of N.A.B. But the third who had relapse is a medical officer of this unit. He is at present having a recrudescence of the trouble though of a much milder degree and is still under observation. His case report is given below :—

Case report

Captain D. belongs to South India. He arrived in East Bengal in September 1943. Started cough in November—after a fortnight began to have breathlessness on exertion and nocturnal wheezing. Had very little expectoration. Symptomatic treatment gave no relief. X-ray of lungs showed fine diffuse mottling. White cell count was 21,400. Differential count: polymorphs—38 per cent, lymphocytes—8 per cent, large mononuclears—0.0 per cent, eosinophils—54 per cent.

Started on N.A.B. injections on 25th February, 1944. 29th February, 1944. Total white cell count—16,250. Differential count: polymorphs—22 per cent, lymphocytes—26 per cent, large mononuclears—1 per cent, eosinophils—51 per cent.

Had eight injections of 0.3 N.A.B. each.

On 15th March. Eosinophile count was 14 per cent. In April condition was much better. Had no breathlessness and no wheezing. In May after the first rains, cough started again. The attack was much milder.

27th May, 1944. Total white cell count—15,000. Differential count: polymorphs—58 per cent, lymphocytes—31 per cent, large mononuclears—1 per cent, eosinophils—10 per cent.

In August 1944 cough was worse. On 12th August, 1944. Total white cell count—19,000. Differential count: polymorphs—20 per cent, lymphocytes—20 per cent, eosinophils—60 per cent.

Had second course of N.A.B. eight injections.

23rd August, 1944. Cold agglutination—negative.

4th September, 1944. Total white cell count—10,000. Differential count: polymorphs—26 per cent, lymphocytes—28 per cent, eosinophils—46 per cent.

18th September, 1944. Total white cell count—12,600. Differential count: polymorphs—22 per cent, lymphocytes—33 per cent, large mononuclears—1 per cent, eosinophils—44 per cent.

November 1944. The cough still persists. Becomes worse during the rains. But much milder than the attacks in 1943. Cough does not prevent him from performing his duties satisfactorily.

From the army standpoint, it is worthy of note that almost all the patients who suffered from pulmonary eosinophilosis were returned back to duty in 6 to 10 weeks after commencement of treatment. If the correct diagnosis had not been made, they would have been evacuated to rear base hospitals as bronchitis or asthma for recategorization or invaliding.

Discussion.—The literature of the subject is very limited. Cases have been observed only for just over a decade. All of them, barring the one reported by Parson Smith from the Middle East, were seen only in India even though the incidence was not confined to any particular race or caste. Frimodt-Møller and Barton (1940) were the first to publish a report on the cases seen by them. The writer has observed this condition from 1936. A series of 81 cases were described in detail by Weingarten (1943) under the title 'Tropical Eosinophilia'. Simeons (1943) recorded 35 cases covering a period of nine years. Treu (1943) reported two cases successfully treated with neoarsphenamine injections. Emerson's (1944) one patient had just returned to America after a stay of 4½ years in India. Chaudhuri (1943) has clearly reviewed the present position concerning our knowledge on the subject, incorporating a report of his own case. One more case was reported by Chakravarty and Roy (1943). Treu (1944) has again reported six cases showing atypical features.

Transient increase of eosinophiles in the blood up to 20 per cent has been noticed in helminthic infections, like ankylostomiasis, hydatid disease, trichiniasis and filariasis. It is also common in certain skin diseases. In eosinophile leukaemia there is very high absolute eosinophilosis with predominance of immature cells. In the condition called Loeffler's syndrome, there is transient high leucocytosis with increase of eosinophiles and mottled shadows in the radiograph of the lungs. It is probably due to infestation of the lung with helminthic larvæ. Besides these, eosinophilia of unknown origin without any disability or disease have also been noticed in certain individuals. The clinical condition now under discussion, however, does not conform to

any of the categories. A high absolute eosinophilia, which persists as long as the symptoms last, is not seen in any other condition. The presence of increased eosinophiles not only in the peripheral blood but also in the bone marrow, the finding of clumps of eosinophile cells in the sputum, the frequency of bronchial spasms, and paroxysmal cough, suggest very strongly a general body response. The nature of the factor that brings about this response is unknown. Some writers are of opinion that it is an allergic manifestation. The presence of bronchial spasms in a number of cases is in its favour. The presence however of general constitutional symptoms like fever and loss of weight, and local symptoms like cough and breathlessness and the constant finding of persistent absolute eosinophilosis point towards an infective process. Carter *et al.* (1944) found mites in 17 cases out of 28 who were suffering from chronic respiratory troubles. In three cases they found leucocytosis and high eosinophilia in the blood. If only they had found eosinophilosis in all the cases in which they found mites in the sputum it could have formed a satisfactory evidence for the causation of pulmonary eosinophilosis. We searched for mites in six cases adopting the technique described by Carter, but our attempts were not successful. Unless and until more extensive investigation is made, one cannot pass any opinion on this interesting finding.

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Pulmonary eosinophilosis

Case number	Cold agglutination, titre	Eosinophiles, per cent	Total white cell count
1	1 : 256	25	15,000
2	1 : 256	32	22,000
3	1 : 1,024	86	30,500
4	1 : 512	56	15,000
5	1 : 512	88	42,000
6	1 : 32	25	15,000
7	1 : 1,024	30	23,000
8	1 : 8	50	14,000
9	1 : 64	23	24,000
10	1 : 1,024	68	34,000
11	1 : 512	24	25,000
12	1 : 1,024	57	22,000
13	1 : 256	23	15,000

Pulmonary eosinophilosis—concl'd.

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16	1 : 16	22	16,000
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18	1 : 128	44	18,000
19	Neg.	25	17,000
20	1 : 1,024	62	35,000
21	1 : 512	62	45,000
22	1 : 64	22	14,000
23	1 : 16	20	15,000
24	Neg.	36	13,500
25	1 : 64	42	25,000
26	1 : 1,024	20	22,000
27	1 : 1,024	30	28,000
28	1 : 1,025	44	50,000
29	1 : 64	58	12,000
30	1 : 64	22	15,000
31	1 : 128	35	14,800
32	1 : 4	20	17,000
33	1 : 128	55	25,000
34	1 : 512	52	32,000
35	1 : 256	68	19,000
36	1 : 8	22	17,000
37	1 : 64	28	21,000
38	Neg.	60	17,000
39	1 : 64	68	32,000
40	1 : 64	30	14,000
41	1 : 64	28	23,000
42	1 : 64	25	20,000
43	1 : 128	48	32,000
44	Neg.	44	14,000
45	Neg.	54	11,000
46	1 : 64	83	56,000
47	1 : 8	30	15,000
48	1 : 16	45	17,000
49	1 : 128	27	21,000
50	1 : 2,048	69	32,000
51	Neg.	59	17,000
52	1 : 16	78	25,000
53	1 : 1,024	50	32,000
54	1 : 512	22	17,000
55	1 : 256	23	21,000
56	1 : 1,024	32	31,000
57	1 : 64	37	22,000
58	1 : 512	54	25,000
59	1 : 64	17	14,000
60	1 : 1,024	69	24,000
61	1 : 16	32	22,000
62	Not done	59	34,000
63	Not done	26	21,000
64	Not done	64	32,000
65	Not done	15	19,000
66	Not done	25	15,000
67	1 : 64	45	18,600
68	1 : 129	28	16,600
69	Neg.	21	17,300
70	1 : 512	19	81,000
71	Neg.	41	24,000
72	1 : 512	16	15,400
73	1 : 32	35	8,200
74	1 : 256	11	18,800
75	1 : 64	58	36,600
76	1 : 512	61	44,400
77	1 : 64	17	22,000
78	Neg.	13	18,000
79	1 : 128	18	14,000
80	1 : 64	17	12,000
81	1 : 1,024	16	21,000
82	1 : 512	31	14,000
83	1 : 1,024	20	11,000
84	1 : 256	14	8,500
85	1 : 2,048	64	34,000

after any one's name, Frimodt-Møller deserves the credit as he was the first to publish a report on the condition. As it has been observed independently by several medical men, impersonal nomenclature will be most appropriate and adequate.

Summary

1. Symptomatology in 85 cases of pulmonary eosinophilosis is reviewed.
2. The acute and the chronic types are described.
3. The constant finding of high-titre cold agglutination is reported.
4. A short review of the available literature on the condition, and a discussion on the aetiology, are given.
5. That it is due to an infection, probably a virus, is also suggested.

My thanks are due to D.M.S. (India) for allowing me to publish the paper, to Colonel M. A. Jaferey for permitting me to study the cases and to Captain B. Natarajan for helping me in the investigation of cold agglutination.

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COMPLEMENT-FIXATION TEST WITH WITEBSKY, KLINGENSTEIN, KUHN (WKK) OR SIMILAR ANTIGENS : AMODIFIED TECHNIQUE

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A TECHNIQUE of a complement-fixation test for kala-azar with WKK antigen was described by Greval, Sen Gupta and Napier in 1939. The value of this test in the diagnosis of kala-azar has been assessed in the subsequent publications by the writer (Sen Gupta, 1943, 1944). In the course of his investigations on the complement-fixation test for kala-azar using antigens prepared from the so-called leprosy bacilli of Kedrowsky and of Lleras, according to the WKK method, during the last two years, the writer has felt that certain alterations in

the technique were advisable in order to obtain the best results with these antigens.

In the technique described by Greval, Sen Gupta and Napier, the maximum amount of antigen not interfering with 1 MHD of complement was determined by titration and this was used in the test proper.

One volume of each of the gradually increasing dilutions, 1 : 10, 1 : 20, 1 : 30, etc., was titrated for anticomplementary activity by mixing with 1 MHD of complement in a volume and one volume of normal saline, and after proper incubation the presence of free complement was detected by adding one volume of sensitized cells and incubating for half an hour.

In the course of investigations it was found that the anticomplementary titre of the antigen was markedly different if instead of one volume of saline one volume of 1 : 25 dilution of a known inactivated non-anticomplementary negative serum was used during the titration of the antigen. The titre was very much lower when the titration was carried out in the presence of 1/25 dilution of the serum in the amount that is present during the test proper. Also the titre was higher in the presence of volume of serum in 1/100 dilution, and highest in the absence of any serum. The amount of antigen and complement free to react was different in the two dilutions of serum used in the test proper, and some slight irregularity was seen in some of the results obtained.

It was therefore decided to titrate the antigen for anticomplementary titre in the presence of 1/25 dilution of a 'negative' serum, to use only 1/25 dilution of the serum in the test proper (this ensures 'specificity' for kala-azar), and to modify the method of titration of the complement. To bring out the differences in the degrees of complement fixation it was decided to use the standard method of using two strengths of complement as in the Wassermann test. The sensitized sheep-cell suspension was prepared in accordance with the requirements of Wassermann test, method no. 4 of Medical Research Committee (1918) with the exception that the sheep-cell suspension was standardized according to a method described by Greval *et al.* (1930).

The technique that has thus been evolved has been tried in a large series of cases and has been found to be quite satisfactory. A brief description of the technique is given below :—

1. *Titration of the antigen.*—0.1 c.c. of the benzolic solution of the antigen is taken up with a 1 c.c. pipette and spread on a glass mortar and allowed to dry completely. 0.2 c.c. of normal saline is then added to the residue in the mortar and a suspension is made by trituration. This forms the starting point for making the dilutions 1/10, 1/20 upwards.

In a series of test tubes labelled to show the dilutions, 1/20, 1/30, 1/40, etc., up to 1/90, put 0.25 c.c. of the corresponding antigen dilution, 0.25 c.c. of 1/25 dilution of an inactivated negative serum, and 0.25 c.c. of complement dilution containing 1 MHD. Mix by gently shaking the tubes. Keep at room temperature for half an hour, then at 37°C. for half an hour. Add 0.25 c.c. of sensitized cells to each tube, mix,

incubate at 37°C. for half an hour; read for hæmolysis. The strongest dilution of the antigen permitting a complete hæmolysis corresponds to the anticomplementary activity short of 1 MHD of complement, and this is the dilution of the antigen to be used in the test proper.

This dilution is then tested for hæmolytic activity by incubating 0.75 c.c. of this dilution with 0.25 c.c. of sensitized cell suspension. The antigen is usually found to be non-hæmolytic.

The power of fixation of the antigen is tested by putting up comparative tests with a series of known sera using a known antigen and the new antigen.

Supposing that 1/60 is the working dilution arrived at by titration, in order to make up the dilution needed for the test proper, a total of 12 c.c. of saline will be required for the residue left after evaporation of 0.1 c.c. of the benzolic solution.

The titration of the antigen is not repeated daily, but the method of titration of the complement and the putting up of an antigen control during the test proper, serves to check the correctness of the antigen titre.

2. *Titration of the complement.*—1 : 10 dilution of the complement in normal saline is first prepared. From this 1/20, 1/30, 1/40, 1/50, . . . 1/120 dilutions are made. Two rows of tubes are set up on a rack to correspond to these dilutions of the complement. Two tubes, one behind the other, correspond to each dilution. In the tubes of the first row are placed 0.25 c.c. of the corresponding complement dilution and 0.5 c.c. of normal saline. In the tubes of the back row are put 0.25 c.c. each of the corresponding complement dilution, 1/25 dilution of inactivated negative serum, and the working dilution of the antigen. The tubes are kept at room temperature for half an hour, then incubated at 37°C. for half an hour. Then 0.25 c.c. of sensitized sheep cells is added to each tube and these are incubated at 37°C. for half an hour, after which the minimum hæmolytic dose (MHD) of the complement is read. This is taken as the highest dilution at which there is complete lysis of the sheep cells. The tubes in the two rows usually show a similar degree of lysis. If there is a disagreement in the titre as indicated in the two rows, this is usually due to the defect in the antigen dilution, and can be rectified by again titrating the antigen against 1 MHD of complement in the presence of 1/25 dilution of a negative serum, and using the antigen in the new working dilution thus obtained.

3. *The test proper.*—The serum to be tested is inactivated to destroy the complement by heating to 55°C. for half an hour in a water bath. 1 : 25 dilution is prepared by mixing 0.1 c.c. of serum with 2.4 c.c. of normal saline.

The antigen dilution is made up as described previously (*vide supra*).

Two strengths of complement dilution are made so as to contain 2 MHD and 5 MHD in a volume. Suppose 1 : 80 is the titre (MHD) of the complement, a 1 : 40 solution of the complement will contain 2 MHD and a 1 : 16 solution 5 MHD in a volume.

Three tubes, placed one behind the other, are required for testing each serum; the first tube is for serum control with 2 MHD of complement, the second and the third for the test with the antigen and 2 and 5 MHD of complement respectively.

An ensemble

- Tube 1. Serum 1/25 dilution 0.25 c.c. + normal saline 0.25 c.c. + 2 MHD complement in 0.25 c.c.
- Tube 2. Serum 1/25 dilution 0.25 c.c. + antigen dilution 0.25 c.c. + 2 MHD complement in 0.25 c.c.
- Tube 3. Serum 1/25 dilution 0.25 c.c. + antigen dilution 0.25 c.c. + 5 MHD complement in 0.25 c.c.

Mix, leave at room temperature for half an hour, then in an incubator at 37°C. for half an hour.

Add sensitized sheep cells 0.25 c.c. to each tube, mix; incubate at 37°C. for half an hour. Read for hæmolysis.

The following general controls are put up along with the test proper:—

1. Antigen control: 0.25 c.c. of each of the following: antigen dilution, 1/25 dilution of negative serum, 1 MHD of complement.
2. Negative serum control: same as 1 but 2 MHD of complement is used.
3. Positive serum control: a known positive serum put up as in the test proper.
4. Cell suspension control: 0.25 c.c. of cell suspension put up with 0.75 c.c. of normal saline.

The method of recording the results of the test

The degree in inhibition of hæmolysis in the different tubes is read as follows:—

Complete inhibition of lysis	=	+	positive.
A trace of lysis	=	T	} doubtful.
More than a trace of lysis	=	±	
Almost complete lysis	=	? -	} negative.
Complete lysis	=	-	

A trace of lysis is detected by leaving the tube in a refrigerator overnight to allow the cells to settle down to the bottom of the tube.

The control tubes 1 and 2 should show complete lysis; the positive serum control should show no lysis with 2 and 5 MHD complement; the cell suspension tube should show no lysis.

Any serum that shows any inhibition of lysis in the serum control tube is to be regarded as anticomplementary; the other tubes are of no value; no opinion as to fixation of the complement by this serum in the presence of antigen can be given.

With complete lysis in the serum control tube, complete inhibition of lysis with 2 MHD of complement along with complete or almost complete inhibition (?T) with 5 MHD is reported as 'strongly positive'; complete inhibition of lysis with 2 MHD, with partial or no inhibition with 5 MHD, is reported as 'positive'; a trace of lysis or partial lysis with 2 MHD, with partial or no inhibition with 5 MHD, is reported as 'doubtful'; and complete or almost complete lysis with 2 MHD complement as 'negative'.

Significance

As pointed out in the previous publications on the subject of complement-fixation test for kala-azar by the writer, in the absence of severe (lepromatous) leprosy and post-kala-azar dermal leishmaniasis, a positive or strongly positive reaction with this test is indicative of kala-azar. It should be borne in mind, however, that a very small proportion of clinically obvious cases of chronic pulmonary tuberculosis gives a positive reaction. This is not a serious drawback. The doubtful reaction is regarded as an indication for further clinical and parasitological investigation. A negative reaction almost rules out kala-azar except in some very

early cases. A negative reaction is obtained in only about 1 per cent of all untreated cases of kala-azar seen in Calcutta.

The advantages of this technique

This technique has the advantage that the antigen and the complement are titrated under the exact conditions that exist in the test proper. The titrations are carried out in such a way that there are exactly 2 and 5 MHD of complement free to react. The adoption of the serum dilution of 1:25 ensures 'specificity' of the test for kala-azar as in the previous technique described by Greval, the writer and Napier. The use of two strengths of the complement in differentiating the degrees of positive reaction is in line with the standard British methods of the Wassermann test. Also, this technique is much less time-consuming than the previously described method, because only one dilution of the serum has to be made. The amount of complement required is somewhat more.

The writer is thankful to Dr. Dharmendra, officer-in-charge of the Leprosy Research Department, and to Mr. R. Bose, the chemist of the same department, for kindly preparing for him several batches of the antigens from the different acid-fast bacilli.

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A CULTURE MEDIUM FROM GROUND- NUT MEAL

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and

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ACTON *et al.* (1932) used a vegetable medium from a green variety of mung dal (*Phaseolus mungo*) for cultivation of the intestinal bacteria. Brewer (1943) suggested a mixture of soya bean and cotton seed or peanut meal for the preparation of a general purpose media using sodium sulphide as an activator; the sodium sulphide would readily generate sulphuretted hydrogen which by lowering the pH of the medium facilitates enzymatic proteolysis.

[Recently, Gottschall (1944) has noticed that during the digestion of meat, papain is activated by a sulphhydryl group from the meat substrate and therefore no preliminary activation is required.]

Groundnut is a good source of certain minerals and vitamin B complex (Pickett, 1942) particularly nicotinic acid; the meal obtained after extraction of oil contains a high percentage of protein body rich in certain essential amino-acids such as arginine, histidine and lysine (Basu, 1943) and it has been shown by Basu and Sen Gupta (1944) to undergo peptonization under the influence of various proteolytic enzymes. It was therefore considered that this meal might be used for preparing a medium for the cultivation of various organisms. The peptonization, however, is variable, but it can be easily increased by an activator. We have found sodium thiosulphate to serve this purpose quite well. The growth-promoting power of the medium might be further potentiated by the incorporation of a liver digest which is a good source of accessory growth factors.

Experimental

Groundnut meal.—The hydraulic-pressed cake of groundnut as available in the market was powdered in a pebble mill, passed through a 60-mesh sieve, dried and stored in a glass-stoppered bottle, special attention being paid to cleanliness in the whole process. The powder is fragrant and palatable, and consists of protein 49.6 per cent, ether extract 6.2 per cent, carbohydrate 22.08 per cent, fibre 5.6 per cent and ash 5.8 per cent.

Preparation of the basal medium.—150 gm. of the above meal powder containing 8.36 per cent nitrogen was taken in 1,500 c.cm. of water, and 200 c.cm. of Cole and Onslow trypsin extract was added and thoroughly shaken. The mixture was then incubated at 50 to 55°C. for four hours. It was filtered through a fine muslin cloth and the volume was made up to 1,500 c.cm. and the pH adjusted to 7.8. Any precipitate was filtered off and the clear filtrate was analysed for nitrogen content. The average result of analysis from three experiments was 0.4 per cent, or 47.8 of the nitrogen content of the meal.

The oxidizable matter of the above broth was then determined by the usual permanganate method in terms of milligrams of oxygen required for 100 c.cm., and was found to be 1.3 per cent (average). It was diluted with water to contain 0.75 per cent oxidizable matter. The final volume of broth obtained was 2.6 litres. The sodium chloride content of the broth was adjusted to 1.4 (*cf.* Scribner and Krueger, 1937).

Preparation of papain digest medium.—6.0 gm. of papain (Ceylon variety) and 3.0 gm. of sodium thiosulphate were mixed together and taken in about 100 c.cm. of water. This suspension was added to a mixture containing 150.0 gm. of meal powder in 1 litre of water. The volume was made up to 1,500 c.cm., and the pH adjusted to 6. The whole mixture was then incubated at 50 to 55°C. for 4 hours. The digested

mixture was filtered off and the pH adjusted to 7.8. Any precipitate noticed was filtered off and the final clear filtrate was made up to the original volume (1,500 c.cm.). On analysis it was found to contain 0.75 per cent nitrogen, i.e. 90 per cent of the nitrogen content of the meal as compared with only 47.8 per cent with trypsin digestion. It was diluted to 3,000 c.cm. The oxidizable matter in this diluted medium was adjusted to 0.75 per cent as in the previous case by the addition of saline solution. This was then incorporated with 5 per cent as well as 10 per cent liver digest by volume prepared as follows: Beef liver was digested with papain according to the method described by Davis *et al.* (1943), and diluted to contain about 12 per cent solid and about 13.5 per cent nitrogen on the total solid content.

The total yield of broth was 5.2 litres compared with 2.6 litres in the case of trypsin digestion. The strength of sodium chloride in the finished broth was adjusted to 1.4 per cent as before. It was then distributed in tubes and sterilized at 15 lbs. pressure for 25 minutes.

In the preparation of solid medium, agar (2.5 per cent) was added to solidify the medium. This was also sterilized as above.

Bacteriological tests

(a) The growth-promoting power of the broths prepared and the usual meat papain digest medium as regards *B. typhosus*, *B. paratyphosus* A and B, *B. dysenteriae* (Shiga and Flexner), *B. coli*, *V. cholerae*, *Staphylococcus albus* and *enterococcus* was studied. The results are as follows:—

Broth containing oxidizable matter 0.75 per cent, and pH adjusted to 7.8	Growth after 18 hours of								
	Typhoid	Paratyphoid A	Paratyphoid B	<i>B. coli</i>	<i>B. shigæ</i>	<i>B. flexner</i>	<i>V. cholera</i>	<i>Staph. albus</i>	<i>Enterococcus</i>
1. Meat papain digest (control) ..	++	++	++	++	+	++	+	+	+
2. Groundnut meal. Papain digest with 10 per cent liver digest.	++	++	++	++	+	++	+	+	+
3. Groundnut meal. Papain digest with 5 per cent liver digest.	+	+	+	+	±	+	±	+	±
4. Groundnut meal. Trypsin digest	+	+	+	+	±	+	±	+	±

++ = Fair growth; + = Growth; ± = Slight growth.

The colonies were larger and the number of organisms greater in broth no. 3 than in no. 1 (control).

(b) The growth of bacteriophage in broth no. 3 was satisfactory, as lysis occurred readily and completely as compared with the broth no. 1. The quantitative and qualitative esti-

mations of the bacteriophage corpuscles were also satisfactory.

Discussion

Groundnut meal is available in sufficient quantity throughout the year in India. It is very cheap compared with meat, the usual source of protein body for preparing culture media. The groundnut meal can be digested both by trypsin and papain, but in the former case only 47.8 per cent of nitrogen is extracted from the meal under our experimental conditions, whereas about 90 per cent extract is obtained when papain is activated by sodium thiosulphate; in the latter case, if the broth be enriched with a trace of liver extract, double the quantity of broth is obtained.

Conclusions

1. Groundnut meal may be used to prepare a culture medium by digesting its protein matter with a proteolytic enzyme such as trypsin or papain.

2. A better yield of broth from the meal may be obtained if activated papain is used and the broth is enriched with a trace of liver extract.

3. In the cultivation of intestinal bacteria and in bacteriophage work, this broth is found to give results as good as those given by meat papain digest.

Acknowledgment

The authors wish to express their sincere thanks to Mr. S. Sen for his help in this investigation.

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- In more recent times, two factors are held mainly responsible for the causation of this particular variety of cataract: one, heat radiation and the other, infra-red rays. Goldman stated that the cataract was due to absorption of heat radiations by the iris, and the heat was then conducted to the lens; the part of the lens not covered with the iris would remain clear. He showed that the iris of the rabbit absorbed about 98 per cent of the infra-red rays which thus became innocuous; and explained that the cataract in the glass-blowers was caused by continued exposure to heat waves. Goldmann published further experiments to conclude that the heat radiation from the furnace raised the temperature behind the iris, which was responsible for cataract formation. He excluded the infra-red rays from the heat radiations by passing them through iodine

filters. Vogt in 1933 reiterated his opinion first expressed in 1912, and confirmed by Meyer and others, that the cataract was not due to heat waves but to infra-red rays.

The matter being still under more or less active discussion, and being likely to assume some importance in view of the rapid war industrialization, a series of experiments on rabbits were performed to find out, if possible, whether the cause of glass-blowers' cataract was the heat radiations. The scope of this investigation was limited to an enquiry into the following two points :—

1. Can cataract be produced by applications of moderate heat?

2. If it can be produced, does it conform to the type met with in glass-blowers?

For the purposes of applying heat, iodine filters were not used as it was felt that their use introduced an unnecessary source of error. Reliance was placed on the current conception that all bodies at certain temperatures emit infra-red rays (Beaumont, 1936), and that metallic bodies emit them in appreciable quantity only when heated to redness, or more especially when heated to dull red heat. For iron that temperature is 500° to 700°C . (Humphris, 1929).

Experiments were performed on six rabbits kept under similar conditions. The heat was applied to the open eye of a rabbit by means of a piece of iron $3\frac{1}{4}$ inch \times $3\frac{1}{4}$ inch \times $3\frac{1}{4}$ inch attached to a long rod with wooden handle and heated so that it was never dull red hot and the temperature considerably below 500°C . It is therefore assumed that in these experiments heat was imparted to the eye unassociated with infra-red rays. The fact that the cataracts produced were not at all axial also shows that no rays passed through, because otherwise they would have been refracted in their course through the lens and would have produced axial cataract. The time of application of heat was kept constant and the applications were repeated every 24 hours. The results obtained are given in the table.

It will be seen from the table that lenticular opacities developed in all the rabbits, but the time required for their production was variable. The shortest period was 80 minutes, i.e. 16 exposures each of 5 minutes' duration. The longest period was 530 minutes (106 exposures of 5 minutes each). In the majority the period was between 180 to 300 minutes.

The type of cataract produced was invariably in the cortex* near the periphery. The shape was variable. In two cases the cataract was sector-shaped, in three it took the form of rounded specks, while in the last it was feather-shaped. In all but one, the opacities produced were permanent. In the exceptional case it

disappeared entirely in about a month after cessation of heat.

TABLE

Serial number	Time required for cataract production	Type of cataract	Shape of cataract	Permanent or temporary
1	$36 \times 5 = 180$ mts.	Peripheral cortical.	Feather-shaped.	Permanent
2	$16 \times 5 = 80$ mts.	"	Rounded specks.	Temporary
3	$40 \times 5 = 200$ mts.	"	"	Permanent
4	$106 \times 5 = 530$ mts.	"	"	"
5	$42 \times 5 = 210$ mts.	"	Sector-shaped.	"
6	$92 \times 5 = 460$ mts.	"	Rounded specks.	"

No changes in the fundus or vitreous were noticed in any animal. All animals suffered from conjunctivitis after varying intervals; if the heat was discontinued, this rapidly subsided in three or four days. In time the animals became accustomed to heat, and the attacks of conjunctivitis became increasingly rare.

It is clear from the above experiments that permanent lenticular opacities can be produced by heat waves of moderate intensity unassociated with infra-red rays, but that heat cataract so produced is a different entity altogether, and that glass-blowers' cataract cannot be produced experimentally at least by heat alone.

Summary

A brief survey of the subject of glass-blowers' cataract is given, and the various views regarding the agent responsible for its production discussed. An account is given of a series of experiments performed on rabbits in this connection. From the results of these experiments it is concluded that permanent cataractous changes in the lens can be produced by heat of moderate intensity when it is unassociated with infra-red rays, and that the cataract so produced is a separate entity altogether, not conforming to the type of glass-blowers' cataract.

I wish to express my thanks to Professor M. Bashir and Dr. R. A. Sayyed for much help and guidance, to Professor M. A. H. Siddiqui in whose laboratory the experimental work was done, and to Professor A. N. Goyal for permission to keep the experimental animals in his department.

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*It is important to note whether the anterior or posterior cortex is involved. An illustration of the opacities would have been useful.—EDITOR, I.M.G.

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A Mirror of Hospital Practice

ALLERGIC REACTION DUE TO MALARIAL INFECTION

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ALLERGIC reaction in man due to malarial infection is of rare occurrence; in recent years, only 6 cases of malarial urticaria have been reported in India, by Chatterjee (1939), Sen Gupta (1942) and Bhowmick (1943).

The following case came under observation at Koraput in Orissa. The place is an inland plateau, 3,000 feet above sea level. It is a hyperendemic place, where *A. fluviatilis* is the main and *A. culicifacies* the secondary vector. All three common malarial parasites are met with, viz, *P. falciparum*, *P. vivax* and *P. malariae*, named in order of their density. The locality is also notorious for presence of blackwater fever.

Case report

Bengalee male, aged 30 years, native of Balasore District, which is another malaria endemic district of Orissa; staying here for the last three years; had had malaria several times in this locality previously but was free from fever for a year or more.

On 22nd November, 1944, at 1 p.m., he was suddenly seized with severe griping pain in the abdomen with nausea, vomiting, and evacuation of bowels twice in half an hour. Then he developed generalized urticaria all over the body accompanied by much itching.

On examination the following were noted:—

Temperature 99°F., pulse 92 and respiration 26 per minute; tongue moist and clean; spleen and liver not palpable; no abdominal tenderness; eyelids much swollen; conjunctivæ highly congested; arthralgia of the knee, elbow, wrist and ankle joints; stool showed no abnormality; no deviation from the usual diet on the previous day; no family or personal history of allergic diathesis was present.

He was given an adrenalin injection and a mixture containing calcium, bismuth, belladonna and mucilage, which helped him to attend his duties next day.

But on the day following, i.e. on 24th November, he had reappearance of the symptoms, with temperature 104.2°F.

Blood slides both thick and thin showed B.T. ring forms and schizonts, the former in large numbers. From 25th morning he was placed on quinine and alkaline mixtures. He had another bout of fever on the 26th with reappearance of all the allergic symptoms. From the next day he became afebrile with

disappearance of all other symptoms and his peripheral blood became free of malarial parasites at the end of the quinine course.

Discussion

The urticaria and other allergic symptoms were no doubt due to vivax malaria and they responded to quinine. Adrenalin and calcium gave immediate relief but did not effect a cure.

Allergic reactions appeared only during the sporulation of *P. vivax* with liberation of merozoites, waste products of the parasites, and remnants of the ruptured red cells, and that only when the number of parasites reached or exceeded the fever level in blood. Before the clinical manifestation of fever, in the incubation or prodromal stage, there was no symptom whatsoever.

The patient had had malaria in his childhood as well as in adult life, but he had never before such symptoms. No family or personal history of allergic diathesis is present.

Summary

A case is reported showing allergic reactions in the form of urticaria, arthralgia, congested eyes, nausea and griping due to *P. vivax* infection and coincident with the time of sporulation of the parasites.

Acknowledgment

I am thankful to Dr. J. N. Das, Civil Surgeon, Koraput, for permitting the publication of this report.

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ALLERGIC MANIFESTATIONS AFTER SULPHATHIAZOLE

By ZAHUR AHMAD QURAISHI, L.S.M.F. (Ph.)

Medical Officer, Thaska Miranji, District Karnal

BERRY recently reported the occurrence of angioneurotic oedema after giving sulphathiazole to a patient. I have also come across such a case.

A Muslim lady, 60 years old, was given 'cibazol' for lupus erythematosus 2 tablets three times a day. In the same evening she developed itching all over the body, more marked on the scalp, face, forearms and hands. These parts became red and slightly swollen, and her eyes became congested with much watering and swelling of the eyelids. This condition subsided on adrenalin injection, but reappeared next evening with slight fever. Then she stopped taking cibazol. Six months later she again took cibazol, when similar symptoms appeared. This time, however, no adrenalin was injected and the urticaria disappeared only on discontinuing the drug.

She had never suffered during her lifetime from any allergic condition, nor is there any family history of allergy. No other sulphadiazine drug has been given to her.

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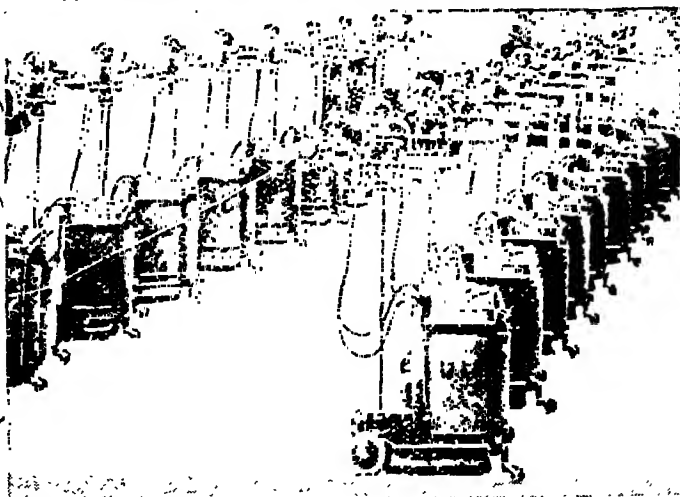
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Indian Medical Gazette

AUGUST

THE TREATMENT OF AMŒBIC DYSENTERY

AMŒBIC dysentery has long been one of the great problems of tropical medicine. During the war of 1914-18, it was a great problem in sub-tropical areas and it became the subject of intensive research. The writings of Dobell on the amœbæ and of numerous writers on treatment, particularly Manson-Bahr, are well known. The general idea became prevalent that the ordinary case of amœbic dysentery could be cured with a combination of emetine by injection, emetine bismuth iodide by mouth and one or more of a number of preparations of arsenic or iodine, the latter sometimes given as retention enemata.

Nevertheless those who have observed the late results of treatment have often been dissatisfied, and have realized the great difficulty with which this infection can be eradicated. During the present war the problem of amœbic dysentery has again come to the fore and the inadequacy of our present methods of treatment is being widely realized. This attitude is well reflected in a number of recent papers and publications on the subject of which we will quote two.

At a recent meeting of the Royal Society of Tropical Medicine (held on 16th November, 1944), an interesting paper on amœbiasis with special reference to treatment was read by Dr. Adams of the Liverpool School of Tropical Medicine. He discusses amœbiasis in Europeans in the tropics. He mentions that workers consider *E. histolytica* as sometimes non-pathogenic but that the detection of *E. histolytica* even in the absence of definite clinical symptoms should not be neglected. He discusses the detection of *E. histolytica* in the stools recording the opinion that several months' practice and specialized training is necessary for real efficiency. He considers that the concentration and cultural methods and complement fixation tests for amœbiasis are hardly worth the time involved.

After discussing the history of treatment of amœbiasis he expresses the following opinion regarding emetine: 'In spite of the choice of emetine compounds available, it appears that some cases of amœbiasis are not sterilized of their infections by the emetine compounds alone, in whatever form and for however long they may be given'.

He discusses the use of bismuth, arsenical compounds, iodine compounds, and considers that while none is infallible each may contribute something to eradicating the infection.

He states that until recently he had thought that the treatment of gut infection with *E. histolytica* had become a matter of simple routine with a few preliminary injections of emetine to control the attack and 3 weeks' blunderbuss assault on the parasites with auremetine, given by mouth and as retention enemata. He himself has used auremetine rather than E. B. I. but holds no strong opinion on their relative values. It was a batch of cases arriving from India and Burma which drew his attention to the inadequacy of present modes of treatment of amœbiasis. In spite of treatment, many of them continued to show parasites and symptoms. New forms of treatment were tried including sulphaguanidine by mouth, rectal administration of various compounds in cod-liver oil, and retention enemata of mepacrine. All produced temporary improvement but none showed a very specific action. He was struck by the fact that many of these cases had before return to England received long courses of emetine, usually several such courses, the number of injections usually varying between 50 and 300 during a period of from 6 months to 2 years. He considers that some of these infections may have become emetine fast. He thinks that unless some more satisfactory form of treatment is discovered than those at present available, chronic post-dysenteric colitis will become an important legacy of the war. The summary of this article is as follows:—

'It is advisable to regard every intestinal infection with *E. histolytica* as pathogenic.

It follows that every detected infestation should be eradicated as early as possible in the interests of the patient. An additional incentive to eradication is the possibility of the dissemination of the infection to others.

Emetine has a more specific action on this infection than any other available drug.

Emetine alone by injection will not sterilize an infection in more than a minority of cases; if it is given unwisely the infection becomes resistant to the drug in all forms and less amenable to any treatment.

Therefore the use of emetine by injection should be restricted to the control of clinically acute manifestations; and the minimum amount necessary to achieve this end should be given.

The eradication of a gut infection must be attempted by the use of a variety of drugs including emetine preparations, all of which have some action on the infection. These drugs should be given together on the grounds that their combined effect is greater than that of any single drug alone, and they must be given as early as possible over an adequate period. Experience has indicated that a 3-week period of such treatment ensures a very high proportion of cures in cases not previously repeatedly treated subcuratively.

When unsuccessful in sterilizing the infection, the course, with, possibly, changes in the preparations of the drugs used, should be repeated

on several occasions as requisite, and without delay, until the infection is ultimately eradicated.

There is an urgent need for fundamental investigation in order to make the testing of new drugs in amoebiasis more scientific and less empirical than it has been in the past.

In the discussion on this paper, several interesting points were brought out by different speakers. Several referred to the value of the sulpha group of drugs in minimizing symptoms by controlling secondary infection without however affecting the amoeba. The occurrence of some persistent and toxic cases going downhill in spite of treatment was reported, with heavy amoebic infection and secondary infection, and the marked action of penicillin in one such case. The occurrence of malnutrition and vitamin deficiency in association with chronic dysentery was mentioned. Manson-Bahr in discussing his well-known treatment stressed the importance of observing the minute details of the treatment. E. B. I. must be given in a form which is absorbed. Retention enemata must not be too big or given too quickly. He was very averse to ringing the changes on all arsenical and other compounds which had been advocated.

The question of two races of amoeba, one pathogenic and one non-pathogenic, was discussed by Hoare.

The paper and general discussion reflected the general dissatisfaction with available methods of treatment of severe amoebic dysentery which is at present so common among British troops.

Another recent publication appeared in the *Lancet* (April 14, 1945) by Lamb and Royston the summary of which is as follows:—

'A series of 81 patients recently returned from overseas has been investigated for amoebic dysentery and those with positive findings treated by mouth with auremetine, carbarsone, or stovarsol, and bismuth subnitrate, and with quinoxyl enemas.

Three fresh and 26 chronic relapsing cases have been treated and the results analysed, the relapse rate in the chronic cases 9 weeks after treatment being 91 per cent.

Thorough treatment of fresh cases is essential if the number ending in chronic ill health is to be reduced.

A new therapeutic agent for the treatment of chronic relapsing amoebiasis is needed.'

In India amoebic dysentery in its more severe and acute forms is perhaps less common in Indians than in Europeans, but nevertheless amoebic infection is the cause of a vast amount of chronic ill health which is caused directly by the infection and secondly by the malnutrition which frequently complicates a chronic amoebic infection or post-dysenteric colitis. Experience teaches us that the infection is most easily eradicated during the initial attack of dysentery. Once a case has become more chronic, eradica-

tion of the infection is very difficult. Therefore thorough treatment of the initial attack is most essential. Unfortunately in many patients the onset of the disease is insidious and the patient is not seen until the infection has been present for a considerable time.

Sigmoidoscopy has become a routine procedure in the diagnosis and management of amoebic infection, and in fact of any dysenteric affection; in acute and sub-acute cases lesions will usually be found within reach of the sigmoidoscope and very often in the rectum.

In chronic cases however with evidence of amoebic infection, sigmoidoscopy is often of less value, the lesions in the lower part of the gut apparently healing up, the persisting lesions being more often in the caecum.

With all the diagnostic and therapeutic measures available and properly used, the diagnosis and treatment of chronic amoebic infection still remains a problem. More studies of this matter are urgently needed.

J. L.

CROSS INFECTION IN HOSPITALS

ONE of the most notable features of medical progress during the war has been the study of cross infection, i.e. infection of a patient in hospital with the causal agent of a disease other than that for which the patient was admitted. When this turns out to be one or another of the specific fevers such as diphtheria, we usually get a clear-cut clinical picture and are able to take measures to minimize its spread, but recent experiences have shown that the danger is not limited to fevers, but extends to many infections of varied nature, which may be manifested clinically or may remain latent and insidiously spread from patient to patient. The problem to-day is how to tackle these cross infections which do not produce unmistakable clinical signs, and hence are not easily recognized as such. They are most apparent and most dangerous amongst infants and young children, and may occur in any hospital, but the risks are greatest in wards for treatment of infectious diseases, and of ear, nose and throat conditions. The subject was lately investigated by a sub-committee of the Medical Research Council, and its report,* though concerned mainly with children's wards, contains recommendations that are equally applicable to all hospital wards, not excepting those containing 'clean' (e.g. maternity and non-infected surgical) cases.

Prevalence

Clinically, cross infection is manifested as a respiratory, gastro-intestinal, wound, skin or

*'The Control of Cross Infection in Hospitals'. Medical Research Council. War Memorandum No. 11. Published by His Majesty's Stationery Office, London. Price, 6d.

mucous membrane infection arising during the course of another disease. The most prevalent type of infection is respiratory, and it may appear as tonsillitis, common cold, otitis media, pneumonia, etc. In infants, it may not assume any of these forms, but gastro-intestinal disturbances may predominate. Undoubtedly the streptococcus is the arch-enemy; its capacity to survive is astonishing. Hæmolytic streptococci and pneumococci are the most frequent causal organisms, and the former may give rise, in addition to respiratory conditions, to a variety of secondary infections such as wound sepsis, puerperal sepsis, erysipelas, impetigo, etc. Gastro-enteritis is one of the oldest scourges in infant wards; although no pathogenic organisms can be found in the majority of primary cases, the secondary form is associated with and possibly caused by infection elsewhere in the body, usually of the respiratory tract and produced by a diversity of bacteria. Bacillary dysentery is not uncommon; it may be severe or appear as mild diarrhoea and the carriers may be altogether missed. Outbreaks of typhoid and paratyphoid occasionally occur from food infected by a carrier among the staff or from transfer of infection from a convalescent patient. Hæmolytic streptococci and staphylococci are the commonest organisms causing cross infection of wounds and various affections of the skin and mucous membranes, that are apt to spread in wards.

Sources and modes of cross infection

As indicated above, the sources of infection may be a clinical or mild unrecognized case, a patient in the incubation period of an infection, or one of those symptomless carriers (convalescent or healthy) who, in outbreaks of certain infections, not uncommonly outnumber the clinical cases, and who may be found among the staff and visitors as well. The infection spreads by means of secretions, excretions and discharges through three main routes, *viz.* contact (direct or indirect), droplet and dust. The part played by contaminated fingers and hands is generally well understood, but it is not sufficiently realized that personal clothes of hospital staff may become contaminated with discharges, etc., during their ward duties, and may thus carry infection to others. Handkerchiefs and the pockets in which they are carried may carry a heavy load of infection when their owners are harbouring pathogenic bacteria in the nose or throat. Ward articles may be contaminated in various ways, and unless sterilized between each use by different patients, there is a risk that they may transfer pathogenic organisms from one person to another. Organisms from the respiratory tract may be carried on thermometers, sputum mugs, spatulas, etc., those from the gastro-intestinal and urinary tracts may be carried on bed-pans, urine bottles, infants' napkins, etc.; while those from wounds and abscesses may be carried

on surgical instruments, dressings, bandages, etc.

The part played by flies and other insects in spreading infection is well known.

Talking, coughing or sneezing can project minute droplets containing bacteria from the mouth and nose for three to six feet through the air. These droplets may directly infect the nose, throat, eye or wound of a person in the close vicinity; they may fall on ward equipment and infect sterile materials or instruments, or they may fall on clothes or on to the floor of the ward where they dry and contribute to the bacterial content of the ward dust. The air of the ward always shows considerable rises in bacterial counts at the time when the dust content is highest, *i.e.* at bed making and sweeping times. Dry sweeping, in particular, raises the dust. It often contains myriads of pathogenic bacteria which may remain alive and infective for weeks, or even months, in a dry state. They come mainly from bed clothes, and are extremely abundant in the dust of wards where patients with upper respiratory infections are being nursed. The dust is inhaled, and the bacteria may become implanted on susceptible tissue and set up infection.

Prevention and control

This consists in the maintenance of a high standard of medical and surgical aseptic nursing technique. As children are particularly liable to cross infection, they should be admitted, if possible, in isolation units. The modern tendency in the construction of children's or infectious disease hospitals is to allow half the number of beds in individual cells, and the remainder in small units. This makes possible the separation of known infected patients. Where cell accommodation is insufficient, selected patients may be nursed in the open ward by the 'isolation nursing' technique. This method of nursing is for the prevention of contact infection only, and will not protect against air-borne and insect-borne infections. It is important for the staff to realize their responsibilities, and for this purpose nurses should be given a short course on practical bacteriology as applied to hospital hygiene, and the kitchen and other staff may be given elementary instruction in hygiene and its relation to their duties. It should be impressed upon them that they must report even minor gastro-intestinal disturbances. It would be well to immunize all members of the staff against enteric and cholera, and periodically examine them especially for ear, nose or throat disease. Personal hygiene should be enforced. As visitors may introduce infection, visiting in children's wards and maternity units should be restricted to a few essential persons only.

To control the various specific modes of cross infection, scrupulous care, cleanliness and disinfection are necessary. It is important

that nurses who change infants' napkins (or otherwise deal with excreta or with septic conditions) should not prepare or give bottle feeds. As breast-fed infants are considerably less prone to gastro-intestinal and respiratory infections than bottle-fed infants, nursing mothers should be given opportunities to continue breast-feeding in hospital. Over-crowding of patients must be avoided. In multiple-bed wards the distance between bed-centres should be not less than twelve feet. Dust is heavily contaminated with pathogenic bacteria, so great care should be taken in handling bed-clothes and no dry dusting of ward floors ought to be permitted.

Conclusions

These findings are the practical outcome of much research work, and throw light on some hitherto obscure conditions. Obviously, the bacteriologist, by throwing his net far and wide, has caught bacteria in unsuspected places and persons, and connected them with many infections which were previously regarded as unrelated events or unfortunate accidents. Clinicians may however wonder if the dangers have not been over emphasized. The evidence of the fact of dust-borne infection is still mostly circumstantial, and it may be questioned whether it is psychologically good to isolate infants and young children in hospital to the point of solitary confinement except for short periods in the case of acutely ill patients. Visitors may be responsible for introducing bacteria in wards, but we know they are often curatively beneficial. But apart from these few debatable points, the recommendations are very sensible and practical. After all, what is aimed at is no more than a high standard of

nursing technique. We too often associate the necessity for extreme care with operation theatres; in ordinary ward work it is apt to be regarded as unnecessary fussiness.

It is known that such infections occur quite commonly in the hospitals in this country although they often escape recognition. How far is it possible to give practical effect to these recommendations in India? Sir Wilson Jameson says 'given good ventilation and bed spacing, the control of cross infection turns largely on three things: adequate isolation accommodation, adequate sterilization and disinfection equipment, and sufficiently trained staff to maintain a meticulously careful technique.' All these are certainly expensive and not easily provided in this country. A larger nursing staff is required, but there is already a serious shortage of nurses. But much can be done with the present staff by training them to practise a good technique rather than wasting their energies on unskilled tasks. Alterations and improvements to buildings can be carried out with the help of engineers, but when new buildings are contemplated, the prevention of cross infection should receive the attention it deserves. There is no doubt that deficiencies exist in most of our hospitals and these should be recognized and action taken as circumstances permit. The remedy lies in the establishment of a perfect routine in the ward work which may range from aseptic dressing of a wound to the proper treatment of soiled linen. It is not a spectacular job, and therefore may not immediately appeal to hospital committees. Yet it affects the health or even life of hundreds of patients.

The subject is worthy of consideration in the post-war medical reconstruction scheme.

R. N. C.

Special Article

CÆSAREAN SECTION

By F. R. W. KINKEAD ALLEN, D.M., M.A.O., M.R.C.O.G.

WITH the modern technique, there is no reason why a woman should not be delivered of at least half a dozen children by cæsarean section; if the first child has been delivered by section, it is possible for subsequent deliveries to take place naturally *per vaginam* provided the operator has avoided sepsis and has repaired the uterine wound properly. The question of sterilization or amputation of the uterus requires very careful consideration. One must consider the parturient's age, station in life, financial status, the number and sex of her children and the possibility that a woman may remain a chronic invalid for life or even die years after-

wards as a result of being left with a latent infective focus in the uterus.

When once an operator has experienced the joy and satisfaction of operating under local infiltration anæsthesia, and has seen the resultant post-operative well-being of both his patients, I doubt whether he will ever willingly revert to other methods of anæsthesia. The sole alleged disadvantage of local anæsthesia is that it is time-consuming for the operator. The advantages are many. Death due to local anæsthesia is extremely rare; hæmorrhage is incredibly small and appears to be less than during normal vaginal delivery; the abdominal wall is completely relaxed; the intestines do not obtrude. The uterus retracts in a manner which is a lesson in itself; closure of the abdomen is

effected without straining or other difficulty; post-operative vomiting and headache are abolished. Immediately on her return to bed the mother can enjoy a cup of tea and then with a hypodermic of 10 mg. morphine drop off to sleep in Sims' posture, thus ensuring that the uterus remains in contact with the anterior abdominal wall without the risk of the intestines or omentum intervening. The infant is delivered with its eyes open, and commences to breathe and cry while awaiting the arrival of the placenta. The placenta separates so quickly that the operator has barely time to clear the mucus and liquor from the infant's pharynx with a piece of gauze on his little finger, and lay the baby between the mother's legs before it is time to lift the placenta out of the wound and hand placenta and child to an attendant.

It is true that the mother may groan and grumble during the incision of the abdominal wall, and may even attempt to draw up her legs or move her hands towards the incision, but these movements are reflexive, and when questioned next day she will deny that she felt any pain. My regret is that I so long delayed following the lead of Macintosh Marshall and others in the employment of local anaesthesia for caesarean section. If a case has been much examined outside hospital before admission, it is advisable to protect the patient by a prophylactic injection of 1,500 international units of concentrated tetanus antitoxin made by a reliable laboratory such as the Haffkine Institute. This should be given either before or immediately after operation.

In some cases, caesarean hysterocolpomy may be indicated; e.g. sepsis, rupture or wound of the uterus too great for repair, occasionally multiple myomata, the unintentional opening of a septic focus such as the intestines, an appendix abscess or an infected dermoid, intractable haemorrhage from an atonic uterus after the placenta has separated, or serious disintegration of the muscular wall accompanying abruptio-placentae. In such cases the transverse incision in the lower segment has the advantage that it forms part of the line of amputation. Carcinoma and occlusion of the cervix call for hysterocolpomy.

Anaesthesia

When time permits, one should premedicate with a hypodermic of 10 to 15 mg. (1/6 to 1/4 grain) morphine to be given between 2½ and 5 hours before the operation is due to commence and followed by 75 to 100 mg. pethidine + 0.3 mg. (1/200 grain) scopolamine 30 to 45 minutes before the patient leaves the ward for the theatre. If morphine is known to excite the patient, if there is placenta praevia or insufficient time, pethidine 75 to 100 mg. + scopolamine 0.3 mg. (1/200 grain) 45 minutes before the parturient is due to be sent to the theatre, and as she is on the point of being taken from her bed, pethidine 75 to 100 mg. + scopolamine 0.15 mg.

(1/400 grain) should be substituted. A serious case of exsanguination may be operated upon on her bed with transfusion running as recommended by Professor S. J. Cameron.

Make preparation for reviving the child, especially if morphine or a barbiturate has been given less than 2½ hours before the operation. Blood transfusion, so important for placenta praevia, should be continued during the operation.

I use pentothal sodium for anaesthesia with some reluctance, because of its effect upon the infant and because haemorrhage from the wounds is as considerable as with inhalation anaesthesia.

Spinal anaesthesia, except in the hands of the very expert, is dangerous for parturient women; if it must be used, the dose should not exceed 1.5 c.c. stovaine or nupercaine hyperbaric (heavy) solution, and the head of the patient should be kept raised on pillows even when she is in the Trendelenburg posture.

Local infiltration anaesthesia with nupercaine (Ciba), which is boilable and produces anaesthesia for 2 hours without inactivating the sulphadiazine drugs, is ideal. The distilled water used for preparing solutions and boiling syringes and needles must have a pH below 7. To secure this, 1 or 2 drops of HCl dil. (B.P.) may be added. Syringes and storage bottles must be of neutral glass. Avoid injecting a vein and reduce the dose for toxic and small women. Have ready 200 c.c. of 0.05 per cent (1/2,000) solution containing 1 c.c. 0.1 per cent adrenalin chloride solution. It is dangerous to exceed this quantity. Unless the nupercaine solution is from the manufacturers' freshly-opened ampoules, the adrenalin must be added immediately prior to the infiltration, to avoid oxidation.

Under the very lightest inhalation narcosis, which may be omitted if as a result of the premedication the patient is sleeping peacefully, bilaterally block thoracic nerves 8, 9, 10, 11 and 12, each with 10 c.c. below and slightly internal to their respective ribs. Infiltrate each iliohypogastric nerve by inserting the point of the needle 2 cm. medial to the anterior superior iliac spine, directing it outwards and slightly cephalad so that it will impinge on the iliacus fascia 2 to 3 cm. below the iliac crest and deposit 10 c.c. through the internal oblique and transversalis muscles along the course of the nerve to where it lies upon the iliacus fascia. It is advisable to place an additional 5 c.c. around each 12th thoracic nerve as it emerges through the internal oblique 2 to 4 cm., depending upon the size of the patient, above the anterior superior iliac spine. If the aim has not been perfect, it may be necessary to infiltrate the line of the incision in the skin and fascia. Using fresh needles, after the abdomen is open, infiltrate 5 c.c. into the extra-peritoneal tissue on each side of the bladder, and 10 c.c. beneath the loose peritoneum covering the lower uterine segment and cervix. By finger pressure disseminate the nupercaine between the bladder

and cervix. Where amputation is to follow, disseminate 5 c.c. into each broad ligament.

Opening the abdomen

It is an advantage to have a vacuum pump to deal with spill and blood, because there is less risk of the infant inspiring contaminated meconium and the adhesions which may result from intra-peritoneal gauze packs are obviated. If local anaesthesia alone is being used, the patient will object to more than gentle traction, and will dislike large intra-abdominal packs, but small sponges with tapes attached or a narrow horse-shoe-shaped roll of gauze can be adjusted under the abdominal incision without discomfort. Leave a catheter in the bladder during the operation. The patient's shoulder should be 15 cm. lower than her pelvis.

Make a 16 to 18 cm. incision in the midline, commencing above the symphysis, but higher, possibly half above the umbilicus, in a huddled case of osteomalacia. Skin towels or rubber dam must protect the wound margins, and a fresh knife be brought into use after the incision in the skin has been completed. Draw the recti and pyramidales laterally, and carefully open the peritoneum. The abdominal wall is sometimes very thin, and the uterus and bladder are immediately underneath. Old adhesions may require attention before satisfactory exposure can be obtained.

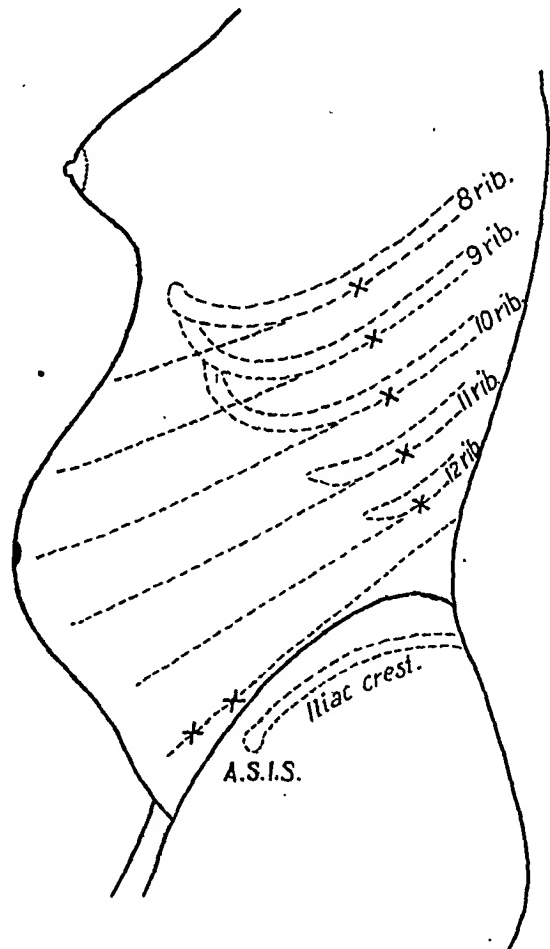


Fig. 1.—Abdominal nerve block to produce analgesia for caesarean section. (Infiltration is to be made at the spots marked 'X'.)

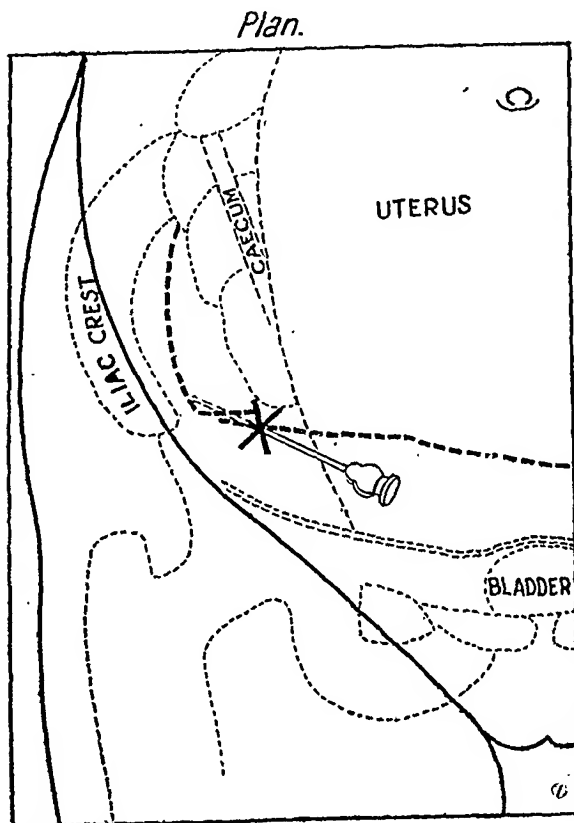


Fig. 1a.

Figs. 1a and 1b show how a needle entered 2 cm. medial to the anterior superior iliac spine can infiltrate the iliohypogastric nerve. (Nerve shown in thick dots.)

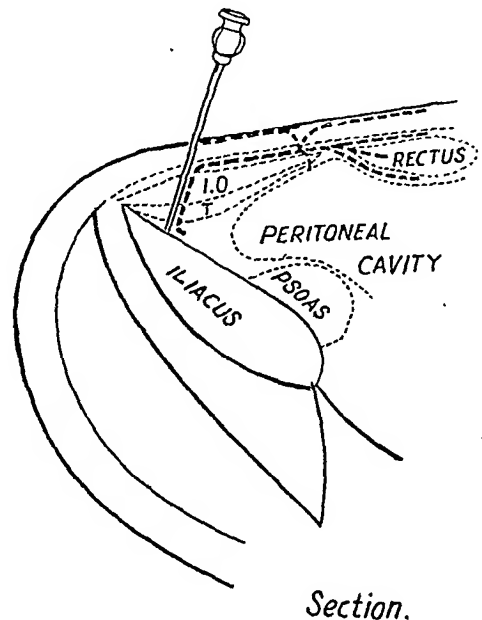


Fig. 1b.

The transperitoneal lower segment operation

Adequate exposure of the vesico-uterine excavation is essential. Verify the area of loose peritoneal attachment, which extends for about

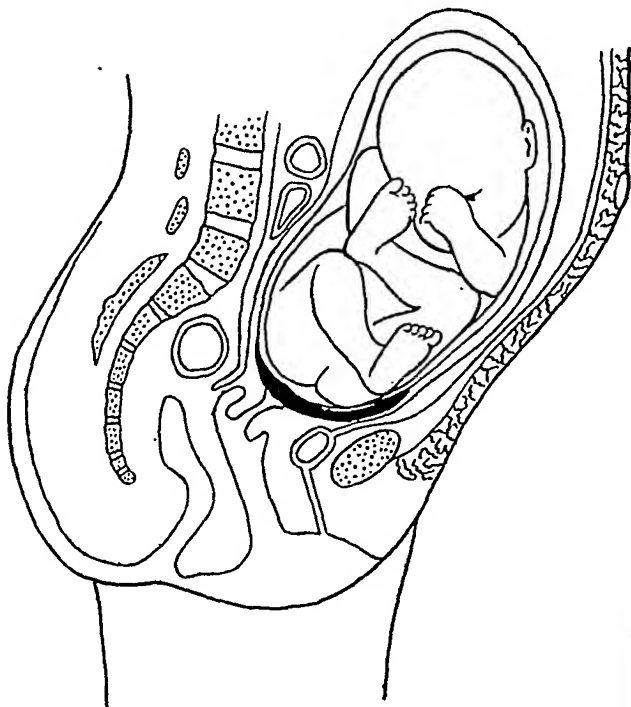


Fig. 2.—Breech presentation, central placenta prævia. Cervix just commencing to dilate, membranes intact.

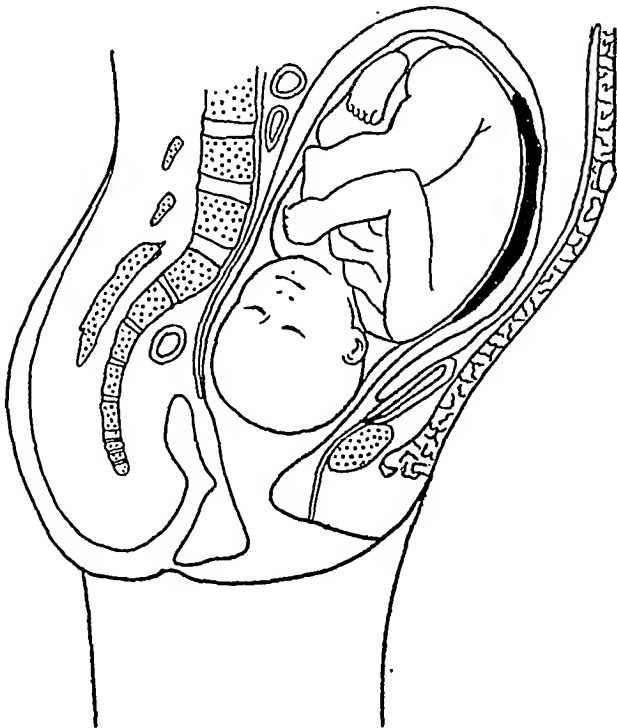


Fig. 3.—L.O.A., cervix obliterated, head engaged in pelvic brim. Soft parts well retracted, membranes ruptured. Note dangerous situation of bladder.

4 cm. vertically, between the lower limit of the corpus uteri and the fundus vesicæ. To aid this, where local anæsthesia is not being employed, 5 c.c. of normal saline may be injected immedi-

ately under the peritoneum. In a frankly septic case, the unopened uterus should be everted, and the abdomen partly closed and walled off by large dry sponges before the uterine incision is commenced. Order an injection of 0.5 mg. of ergometrine into the uterus or the deltoid, but where the presenting part is deeply engaged in the pelvis, postpone the injection of ergometrine until the presenting part is emerging through the incision in the uterus. About 2 cm. proximal to its reflexion from the bladder, make a 12 cm. transverse incision in the peritoneum. By blunt dissection free the peritoneal flaps proximally and distally. The margins of the distal flap may be pinned with a stitch to the skin at the pubic end of the incision. Low in the cervix, map out a 12 cm. transverse incision, but where an anterior placenta prævia is heralded by large veins in the lower segment, or where access is obstructed by deformity of the pelvis, make a vertical incision which will have to encroach on the corpus, and, unless as a result of long labour the lower segment is too thin, at each end insert a long, strong, stay suture. Cautiously cut through the muscle and any placenta prævia obtruding (a Bonney's compressor will minimize the bleeding, which, except under local anæsthesia, is very free) until the amniotic sac is reached. While assistants suck or mop out the spill and hold the stay sutures to steady the cervix against the abdominal wall, enlarge the wound laterally with round-ended scissors cutting between two guiding fingers. Avoid going beyond the stay sutures and wounding the uterine arteries. Bleeding from the cut cervix may be controlled by four Green-Armytage flat tongue or Allis' forceps. Where a vertical incision has been made, intestinal clamps will serve until the spouting sinuses can be closed by Allis' forceps.

In a head presentation, the face or occiput of the infant may be rotated into the incision by inserting a finger in the mouth or by applying an Allis' forceps near the small fontanelle and pulling gently. The mouth and throat of the child may be cleared by vacuum pump or by sponging. In a breech presentation, hook a finger into a groin and rotate it into the incision. Unless the presenting part is deeply engaged, order an assistant to exert gentle pressure on the fundus uteri to deliver the presenting part. If this fails, or if the presenting part is wedged into the pelvis, one or both blades of the obstetric forceps should be used to ease out the presenting part, though a finger in the groin or traction on a leg usually suffices to ease out a breech. Pulling with Willett's or tongue forceps risks tearing away a piece of skin.

As the presenting part is delivered through the cervical incision, order 5 units of 'pitocin' to be injected into the uterus or deltoid. Deliver the rest of the child slowly while uterine contraction and retraction aid extrusion

as in a normal labour. Clear the infant's airway, and if it commences to breathe, place it between its mother's legs. Wait for the placenta to separate, lift the cord to draw the membranes clear, and hand the child and placenta to an attendant with instructions not to cut the cord until it ceases to pulsate. If the child will not respire easily, divide the cord between two hæmostats, hand the child for treatment to the chosen attendant, and wait for the uterus to cast off the placenta before lifting the cord to draw the membranes off the endometrium.

With a large sponge wrung out in hot saline, wipe the interior of the uterus free of shreds of the placenta or membranes. Palpate the cavity for a rupture, myoma, etc. The uterus should be hardening and blanching; if it is too slow, wrap the corpus in a hot damp towel and knead it. If there is uncontrolled hæmorrhage from a placenta prævia, oversew the site in the lower segment. Failure of the uterus to contract should be treated by a second injection of 0.5 mg. ergometrine into a muscle, 0.25 mg. into a vein, or by tightly plugging the uterine cavity with gauze, which will subsequently be removed *per vaginam*, but bear in mind that death may result if this gauze is inadvertently included in the suture line at the time of closure.

Where the uterus is potentially or actually infected and amputation is not desired, lay one end of a 50 cm. (20 inches) length of 2 mm. (1/16 inch) rubber tubing in the cavity of the uterus up to the fundus and push the remainder down to, but not through, the external os, anchor the tube in position with catgut, and insufflate 10 g. sterilized penicillin-sulphathiazole powder into the uterine cavity, the incision, and the vesico-uterine excavation. (At the conclusion of the operation, the end of the rubber tubing will be drawn into the vagina and strapped to the thigh for subsequent instillations of penicillin.)

Except where hysterectomy is to follow, close the incision in the cervix in two layers using continuous 40-day no. 1 catgut. Avoid including the endometrium or the posterior wall of the cervix in the first row; the second row must overlap or at least approximate the fascia. Where there is no danger of sepsis and if you are certain of excluding the endometrium, continuous nylon suture may be employed. Absolute hæmostasis must be attained. Remove the stay suture, and with a continuous thread of finest material close the visceral peritoneum, the upper flap of which may first be anchored by a couple of stitches over the uterine incision.

Where a vertical incision has been made, take the body of the uterus in one hand, and with scissors in the other hand bevel off the endometrium. Appose the muscle and peritoneum only by continuous or interrupted 40-day catgut, or of nylon where there is no danger of sepsis or of including the endometrium. Bury the

knots under the peritoneum, and meticulously coapt the peritoneal margins.

Sterilization

If the woman has had several children of the desired sex or where some special reason exists, exsect the fallopian tubes where they enter the uterus, coapt the gaps in the uterine cornua, and cover them accurately with peritoneum. Bury the cut ends of the tubes in the broad ligament without leaving any raw surfaces to cause adhesions.

Cæsarean hysterectomy

The subtotal operation is relatively simple.

After delivering the infant through the transverse incision in the lower segment, cut the cord between two hæmostats. Unless they separate of their own accord, leave the placenta and membranes *in situ*, and gently eventrate the uterus. Disseminate 5 c.c. nupercaine solution subperitoneally on the posterior wall of the lower segment.

Ligate the round ligaments distally about 2 cm. from the uterus, clamp them proximally and cut between clamp and ligature. Apply two long clamps to each broad ligament on each side of the uterus. Leave the adnexa unless diseased. Cut between the clamps. Similarly apply two more clamps to each broad ligament down to and including the uterine arteries. A separate pair of hæmostats may be applied to the uterine arteries, which can be located by touch, taking care to grasp the tissue at the side of the uterus and thus avoid the ureter which is perilously close. Cut down between the second pair of clamps and, after ascertaining that the uterine arteries are secured, extend the original transverse incision right round the uterus. If the original incision was vertical, amputate the uterus through the lower segment.

Ligate the uterine arteries and place two figure-of-eight ligatures on each broad ligament.

Using catgut, loosely coapt the edges of the lower segment without including the endometrium, push the suture ends through into the cervix to act as a drain, sew the round and broad ligament stumps into the uterine stump, insufflate 5 g. sterilized penicillin-sulphathiazole powder, and unite the peritoneal flaps over the junction. Insufflate 5 g. sterilized penicillin-sulphathiazole powder into the pelvic cavity.

The total operation for carcinoma is a much more formidable affair. The danger of injuring the ureters is increased. If deep x-ray or radium therapy for follow-up treatment will not be available, a Wertheim's hysterectomy should be attempted by the operator if competent. Extra nupercaine infiltration is required right down to the vaginal fornices, and a third pair of long clamps will be required on each broad ligament after the bladder has been completely separated from the cervix. Close the vagina in the same way as described for the lower segment, and unite it to the stumps of the broad and round

ligaments. Cover the junction by the peritoneal flaps.

Closure of the abdomen

Remove and count all sponges, etc. Level up the patient. Dry out the abdominal and pelvic cavities especially the pouch of Douglas. Tuck the free border of the omentum down into the recto-uterine excavation over the coils of intestine. Return the uterus to the abdominal cavity if it has been everted. Close the abdomen in layers. For the skin I prefer to use Allen & Hanbury's 'Auto-skin clips.' Tension sutures are essential.

The supravescical extra-peritoneal lower segment operation

In potentially infected cases, where it is desired to conserve the uterus, the operation may be performed extra-peritoneally. Sterilize the vagina thoroughly. If the presenting part is fixed, push it up well. Insert a self-retaining catheter. Make an 18 cm. midline abdominal wall incision down to the pubis separating the recti and pyramidales. (I prefer a Pfannenstiel incision but for brevity I forbear from describing it.) 30 c.c. of the anæsthetic solution must now be diluted with 30 c.c. sterile water or isotonic saline and a thorough infiltration made under the perivesical fascia and extra-peritoneal tissues over the front of the bladder, on each side of the bladder and in the vesico-uterine excavation, avoid puncturing the peritoneum or bladder. Order an assistant to distend the bladder with aqueous methylene blue solution (usually about 200 c.c. is required) and then to clamp the catheter. Make a 'T' incision in the transversalis and perivesical fasciæ to permit the bladder to bulge forward. The peritoneum is firmly adherent only over the postero-superior surface of the bladder. Draw the fat pad and cellular tissue containing the peritoneum proximally up to this firm attachment, work a scalpel handle or finger tip over each lateral angle of the bladder to separate the peritoneum from its loose attachments. Stretch the central firm attachment; release the catheter clamp to empty the bladder and, working with the edge of a knife or scissors-clipping, detach the peritoneum. Should the bladder be injured, which is not uncommon, it must be repaired in layers. Should the peritoneum be opened, the hole, if small, must be tied off without using a needle, or, if large, repaired in such a manner that there is no puncture left in the peritoneum. Mobilize the remainder of the peritoneum covering the bladder and lower uterine segment by blunt dissection, push the bladder down behind the pubis and hold it there by a large retractor to obtain a sufficient exposure for a 12 cm. extra-peritoneal transverse incision in the cervix. As described under the transperitoneal lower segment operation, make a transverse incision in the lower segment, extract the infant and placenta, and sew up the cervix. It is advisable to dust

10 g. sterilized penicillin-sulphathiazole powder all over the uterine wound and subperitoneal space, and to leave a length of 4 mm. (1/6 inch) rubber tubing down to the vesico-uterine excavation; this will serve as a drain, or, if the case becomes septic, for instilling penicillin. Level up the patient and close the abdomen as already described. Tension sutures are important. A self-retaining catheter should be kept in the bladder for a week if an injury has been done to the bladder wall.

After treatment

To assist involution put the infant to the breast after the operation, the earlier the better.

Immediately after the operation and during the puerperium, the patient should lie and sleep as much as possible in Sims' posture.

If all goes well, she should sit upright on the 3rd day and be out of bed on the 5th day. From the earliest moment, deep breathing, leg exercises and arm exercises in bed are important.

Remove the skin clips or stitches on the 7th or 8th day. If union is not quite satisfactory, dress once daily with finely powdered urea or sodium sulphate to clean the wound, and when clean, apply sterile anhydrous glycerine until healing takes place. Do not remove the tension sutures until the abdominal wound is firmly united; the 10th day is the earliest on which I remove them.

Post-operative retention of urine is usually best treated by giving intramuscular injections of 0.125 to 0.25 mg. doryl, moryl, esmodil or carbachol, which may be repeated up to 3 times in 24 hours. When prescribing the sulpha drugs they should be ordered in sufficient dosage and according to their rate of excretion: sulphathiazole 2 hourly; sulphanilamide 4 hourly; sulphapyridine, sulphadiazine and sulphamezathine 6 hourly; sulphamerazine 8 hourly. Alkalis must be given to keep the urinary pH at 8. Six to eight pints of fluid (3 to 4 litres) in each 24 hours must be given by some route to the patient. The fluid intake and urinary output must be charted to see that the patient is passing 250 c.c. (8½ oz.) every 6 hours. To obviate nausea and vomiting 50 to 60 mg. of nicotinic acid should be given with each dose of a sulpha drug.

For a case of mild sepsis, where a tube has been left in the uterus and where the organisms prove susceptible, during the first 48 hours, instil every 6 hours 5,000 units of penicillin in 5 c.c. sterile distilled water. This may be reduced to twice daily for a further 4 to 5 days if required at all. Where the organisms are insusceptible to penicillin, substitute instillations of sterile anhydrous glycerine.

For a serious case of sepsis due to susceptible organisms, 2 hourly intramuscular doses of at least 12,500 units penicillin or a continuous intramuscular drip ensuring a minimum dose of 100,000 units in 24 hours will be required in addition to instillations.

Distension is best treated by large doses of activated charcoal. For ileus, neither pituitrin nor purgatives should be given. Drainage of the stomach and intestines by means of a Miller-Abbott tube, or in its absence by means of an indwelling Ryle's or Bailey's tube, gives good results combined with intravenous or rectal fluids.

Acute dilatation of the stomach is to be treated by continuous aspiration through a Bailey's or Ryle's tube and intravenous or rectal fluids.

Lochiostasis due to retrodisplacement of the uterus must be combated by Sims' posture or by inserting a finger in the rectum and raising the uterus thereon.

Dehydration must be obviated by giving fruit juice and other drinks in plenty. If the patient is unable to retain fluid by mouth it must be given intravenously and rectally.

If there is diarrhoea, an iron-containing mixture will usually rapidly control the excessive evacuations and improve the anæmia.

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- (4) diphtheria antitoxin, (5) smallpox vaccine, (6) iron, (7) quinine, (8) iodine, (9) alcohol and (10) mercury.

This year, the editor of the *Journal of the American Medical Association* (10th March, 1945, p. 593) asked professors of medicine in teaching medical schools to state the ten remedies which in their opinion were the most important or useful. From the replies to the question the following list was compiled: (1) Penicillin and the sulfonamides and antibiotics. (2) Whole blood, blood plasma and blood derivatives. (3) Quinine and quinacrine. (4) Ether and other anæsthetics, morphine, cocaine and the barbituric acid derivatives. (5) Digitalis. (6) Arsphenamines. (7) Immunizing agents and specific antitoxins and vaccines. (8) Insulin and liver extract. (9) Other hormones. (10) Vitamins.

MANSON OF TROPICAL MEDICINE

Abstracted from the *Lancet*, 6th January, 1945, p. 37

SIR Patrick Manson was born a hundred years ago, and a meeting to celebrate that important event was held on 14th December at Manson House, the home of the Royal Society of Tropical Medicine in Portland Place. His famous diary, in which he recorded in great detail all his main discoveries from 1873 onwards, was on view, with the diary which he kept in Formosa in 1866. Portraits of him at various stages of his romantic career gave spirit to a little collection of exhibits of interest to tropical experts—his drawings of the development of filaria in the mosquito, the actual slides showing development of filaria in mosquitoes sent to Cobbold in 1877, and the slides of malaria-infected anopheles sent to Manson himself by Ross.

Sir Philip Manson-Bahr, in an address, told of his father-in-law's birth on 3rd October, 1844, at the small town of Old Meldrum, near Aberdeen. He spent his boyhood fishing for eels, tickling trout, shooting partridges and playing cricket. When he was 15 he was apprenticed to the firm of Blackie Bros., iron-founders in Aberdeen; but he developed curvature of the spine, and with it that tremor of the right arm which many remember as characteristic of him. While he was lying on his back, recovering from this condition, he decided to take up medicine, and with typical energy qualified while still below the statutory age in 1865.

Next year he went to Formosa, where he was port medical officer for 4 years, earning enough to repay his father the cost of his education. After a few more years spent at Amoy, he returned to Scotland in 1875, and married. Stirred by Lewis's work on filaria in Calcutta, he returned to Amoy with his wife and a microscope, and by 1877 had discovered the nocturnal periodicity of filaria. Of his two Chinese assistants, the one who worked at night always found the parasite. 'It is the discrepancy which teaches, if you would learn', Manson said. In 1878 he demonstrated the life-history of the filaria in the mosquito, news of which he sent in a modest letter, accompanied by specimens, to Cobbold in London. His study of parasites from that time progressed rapidly. In 1883 he was appointed dean of the Hong Kong Medical School, which he helped to found.

In 1890 he went home to Aberdeenshire, but in the following year, owing to a fall in the value of the Chinese dollar, he returned to practise, this time in London, where he formed the nucleus of what was to become the London School of Tropical Medicine. His studies of filaria grew and prospered. In 1894, arguing by analogy from what he had observed in filaria, he formulated his mosquito-malaria theory, and acquired the nickname of Mosquito Manson among the colleagues. Ronald Ross, then a major in the Indian Medical Service, got into touch with him, and in a famous correspondence of 58 letters (which Ross thought 'as noble a series as ever a man received')

Medical News

THE MOST IMPORTANT DRUGS

(Abstracted from the *Pharmaceutical Journal*, 21st April, 1945, p. 203)

IN 1910 the following drugs, in the order given, were listed by United States physicians as the most important: (1) ether, (2) morphine, (3) digitalis,

the malaria problem was thrashed out. In an experiment designed to convince the British Government, Manson arranged for anopheles infected with benign tertian to convey the parasite to his eldest son by their bites. Patrick Thorburn Manson, then a medical student at Guy's, duly developed the disease.

The London School of Hygiene and Tropical Medicine was opened under Manson's direction in 1899; he retired in 1912 and died in 1922, after some happy years spent mainly in fishing in Ireland.

SCIENTIFIC RESEARCH IN INDIA

TOWARDS the end of 1943 Professor A. V. Hill, F.R.S., visited this country to advise the Government of India on the organization of scientific and industrial research and its co-ordination with the corresponding activities in England and other countries. His report, *Scientific Research in India* (Government of India, Simla, price 8 annas), is a valuable document and should be widely read.

At the outset Professor Hill referred to the lack of scientific liaison between Britain and India in contrast to the actions taken by the Dominions and the U.S.A. not only for war purposes but also for co-operative relations after it, with the result that India has been needlessly isolated and that her scientific and technical resources have not been utilized or developed to anything like the same degree as those of the other major countries. One of the most urgent needs is for young teachers, research workers and members of the technical staffs to be provided with facilities for advanced study abroad. For this, arrangements should be made in good time in view of the expected overcrowding soon after the war. Only the ablest people should be selected; financial assets of their fathers or a decision to get a higher qualification as a step to advancement in a profession should not weigh in selection. It is advisable to set up in London an Indian scientific office to deal with scientific matters and help workers coming from India, and the president of the Royal Society has expressed willingness to set up a standing sub-committee of the Society to afford general scientific assistance on Indian affairs.

Medical education

There are many medical colleges in India, but their standard seemed to Professor Hill to be unduly low. Routine teaching is done to a moderate standard limited by staff, space and equipment. No real improvement can take place until most members of the staff hold full-time appointments and are reasonably well-paid; at present they are apt to be busy medical practitioners, who, for a meagre part-time salary, come in and take a turn at teaching the classes. No great school of physiology has ever developed in India from which teachers and research workers could go out to other schools and raise the standard all round. This applies to most other subjects connected with medicine. No research work of any significance in clinical medicine is yet done in the colleges. There are very few full-time teachers and research workers in the clinical subjects, and there are no full-time medical, surgical or gynaecological units. Busy and successful practitioners usually control the teaching and stand out as the ideal to be aimed at by the medical student. India has a very high tradition in connection with tropical medicine, but the work has been done mainly outside the departments of the medical colleges, which remain largely adjuncts of medicine for routine examination and teaching. Research can reproduce itself only if it is in contact with students and young graduates.

An all-India medical centre

The most effective way of making a change in all this would be to create teachers and research workers

able to devote their lives to the advancement of science and practice of medicine. For this purpose, an All-India Medical Centre should be established, an 'Indian Johns Hopkins', staffed by the ablest people available anywhere, employed full-time and adequately paid, and the best possible students should be brought into the centre with financial help, if necessary, in the form of scholarships. A special hospital should be attached to it for the study of malaria in which India has already played a large part.

Medical research

This is mainly carried out at special institutes in which very distinguished work has been done, particularly in tropical medicine. Among them are the Central Research Institute at Kasauli, the School of Tropical Medicine at Calcutta, the Haffkine Institute at Bombay and many others. By this arrangement the workers are not unduly burdened by teaching and routine, but there is the disadvantage in isolating medical education and the clinical work of teaching hospitals from all contact with research. The existing institutes should be brought, where practicable, into closer contact with the medical colleges and higher medical education. Compared with the British Medical Research Council, the Indian Research Fund Association, has very limited functions, chiefly owing to scarcity of funds.

Miscellaneous

Professor Hill then deals with other subjects, but we have space only to refer to a few points. Scientific research in universities is the basis of all scientific progress, but except in few subjects very little has been done. In the biological sciences, the university departments are no better than the medical colleges already referred to. The modern physiological or functional approach to zoology is almost completely absent. There is very little original work of any kind going on genetics. Biophysics is almost completely absent, except at the Bose Institute in Calcutta which is not a department of the university. Biochemistry is quite strong in some centres, but tends to be associated with chemistry rather than physiology, zoology or botany. Except in one or two centres, physiology has no place except outside the medical colleges, in spite of its importance for general education.

Science has played a large part in the present war and will probably play a still greater part in future conflicts. A proper scientific organization must be built up within the war department itself. The material resources of India are very great, but most inadequately known; this is a hindrance now in the war effort of the country. The foundation in 1940 of the Board of Scientific and Industrial Research represented a very notable step forward in the organization of Government science in India; its full influence has not yet had time to be felt. Real research pays, but Indian industry as a whole has not yet appreciated the degree to which it pays. The Metallurgical Laboratory of the Tata Steel Works at Jamshedpur is probably the nearest approach to the American and British model. The manufacture of scientific instruments and apparatus (including surgical instruments and equipment) should be encouraged. A very high standard should be adopted from the start. Finally Professor Hill suggests a central organization for scientific research of which a sketch is given in the report.

V.D. LECTURES FOR NURSES

A SMALL pamphlet *V.D. Lectures for Nurses* written by Dr. Reynold H. Boyd has been published by William Heinemann Medical Books, Ltd., London. It contains a brief account of venereal diseases followed by a few practical notes on avoidance of infection in nursing, on taking smears and blood and on preparing for injections and lumbar puncture. Price 2s. net.

Public Health Section

THE PROBLEM OF ENDEMICITY OF CHOLERA IN BENGAL

(A PLEA FOR FURTHER INVESTIGATION)*

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IN no country in the world to-day or perhaps at any time has cholera been so prevalent as in India and particularly in Bengal. The latter has been declared the permanent endemic home from which many of the epidemics and most of the pandemics of cholera have originated. Cholera forms one of the most important gastro-intestinal diseases which, next to malaria, takes the heaviest toll of life every year in Bengal.

In spite of the discovery of *V. cholera*, the causative agent, by Koch as far back as 1883, and of the subsequent other studies by Pfeiffer, Metchnikoff, Pettenkoffer and others, and of the introduction of preventive inoculation initiated by Ferran (Med. Res. Council, 1929) in Spain and followed by Haffkine (1895) in Bombay and later improved by Kolle (1896), the knowledge regarding the epidemiology and control did not improve as fast as in many other infectious diseases. The gap was, however, greatly bridged by some outstanding work such as that of Roger's re-establishment of saline treatment, Greig's method of differentiation of hæmolytic and non-hæmolytic strains, d'Herelle's discovery of bacteriophage and perhaps a few other discoveries not so important. Undoubtedly there has been a falling trend in the mortality from cholera in India due partly to the introduction of anti-cholera vaccination and partly to the growing activities of the public health department which is still in its infant stage; the achievement has not so far, however, been significant.

The almost static condition of cholera research a few years ago was perhaps due to the fact that except for the accidental introduction through communications, travel and pilgrimage, etc., it had never been a matter of great concern for the Western World where the sciences of bacteriology and epidemiology originated, developed and are being vastly improved. It is mainly an Indian problem and it should have been a matter of concern for the Indian government, the Indian public and Indian scientists.

The importance of the problem, as well as of the desirability that India with her special

facilities for field investigation should undertake the research on a large scale in the light of the newer knowledge in bacteriology, was after all recognized by the Cholera Sub-Committee at the 11th Medical Research Workers' Conference held in December 1931, and was also pointed out by the Office Internationale d'Hygiène Publique, Paris. As a result, the Indian Research Fund Association instituted a Special Advisory Committee to co-ordinate research work on cholera, and in 1934, several enquiries were started at various institutional centres, viz Calcutta, Madras, Shillong and Kasauli, in addition to those enquiries already in progress for some years. These enquiries carried out investigations into different aspects of the problem for varying periods, and most of them terminated by the year 1940. The writer himself had the opportunity of serving in several of these enquiries for a period extending over more than five years. The following aspects of the problem were particularly investigated:

- (1) The serology of vibrios.
 - (a) Inaba and Ogawa types.
 - (b) The El Tor vibrio and vibrio hæmolysin.
- (2) Biochemical reactions.
- (3) Chemical structure and metabolism of the vibrios.
- (4) Cholera toxin.
- (5) The biochemistry of cholera case.
- (6) Differential isolation of vibrios.
- (7) Survival and multiplication of *V. cholera* in water.
- (8) Statistical investigations.
- (9) The forecast of cholera.
- (10) The epidemiology and the carrier problem.

The ultimate purpose of these investigations was to solve the problem of epidemiology (both epidemicity and endemicity, particularly the latter) of cholera so that effective control measures could be evolved with the final object of complete eradication of the disease, if possible, from its endemic home whence the infection is supposed to spread regularly. While the results of these investigations are supposed to have clarified many fundamental issues and advanced our knowledge on the various aspects of the problem, including the technique required for their studies, it is to be seen how far the studies have been helpful in the solution of the main problem 'endemicity'. For a complete survey of the results obtained in these investigations the readers are referred to the review on the subject 'Cholera Research in India, 1934-40' by Major-General Sir John Taylor, late Director, Central Research Institute, Kasauli, India.

* Read before the Annual Conference of the All-Bengal Public Health Association held at Calcutta on the 25th October, 1944.

Present position of the epidemiology and carrier problem in cholera

The bulk of the evidence collected before the commencement of the above investigations tended to show that in cholera the 'carrier' did not exist in the same sense as in typhoid or dysentery. *V. cholerae* was found to persist in convalescents and contacts only for a short period, and it was therefore thought unlikely that the carrier was responsible for transmitting infection at any prolonged interval after the primary infection and consequently to places remote from the cholera-infected areas. The other important possible source of infection was contaminated water. Both the questions were obviously of importance in relation to the epidemiology of cholera. The investigations under the I. R. F. A. therefore aimed mainly at the studies of these two factors, viz (1) the question of the carrier and (2) the position of *V. cholerae* in the environmental sources, particularly water.

Among the primary difficulties that were encountered the following should be mentioned :

(1) What is a true cholera vibrio? Is the vibrio really responsible for cholera? What is the definition of cholera? Should it be based on bacteriological findings or on clinical findings?

(2) Are the existing methods of isolation of the organism adequate? If not, what is the best method of recognizing the true cholera vibrio?

(3) What is the relationship of the true cholera vibrio, if defined, to the other types of vibrio found in human beings, in water, etc.?

It was recognized that unless these basic points were settled beyond doubt, no progress could be expected in the investigations of the epidemiology of cholera, which involves the relationship of the vibrio to the cholera case and to the epidemic, whether occurring in the endemic or non-endemic areas, and investigations of the conditions under which *V. cholerae* exists and is transmitted as an infecting agent. The necessity for identifying true cholera vibrios was further emphasized by the findings as to the common distribution of various serological and biochemical types in natural waters in the plains of India and in various other sources. It was also of interest therefore to study the relationship of the former to the latter types of vibrio which might play some rôle in the epidemiology and particularly in the endemicity of cholera. Also, without the clarification of these points, it was not possible confidently to recommend the proper strain for the preparation of vaccine for preventive inoculation and effective quarantine measures.

From the results of the above investigations, attempts were made to establish that only one type of vibrio, viz serological type O sub-group I of Gardner and Venkatraman (1935) was the cause of cholera, and this conclusion was accepted as the working hypothesis by the Office

Internationale d'Hygiène Publique, Paris. A differential medium had also been found (Read, 1939) in the preparation and trial of which the writer himself (Seal, 1939) took an active part. Accordingly, the significance of the results of the earlier field and laboratory investigations was open to doubt. After the working basis had been established, the ideas about the epidemiology of cholera were provisionally re-oriented, and the later field enquiries in an endemic area of Bengal were inaugurated to obtain more exact information as to the distribution of *V. cholerae*, as defined, and to its relation to the cholera case and eventually to other factors in epidemiology. The problem as to how cholera infection persists in an endemic area was taken up in these field enquiries having in view the following points :

(a) Direct transfer of the vibrio from case to case.

(b) Persistence of the vibrio in the cholera convalescent or healthy carrier.

(c) Survival of the vibrio, with or without multiplication, in infected water.

The Bengal Cholera Field Enquiry in which the writer also served for some time was established on the above basis in regard to the diagnosis of *V. cholerae*, and the newer technique developed for differential isolation of the vibrios was employed. Thus the entire attention was then directed towards the study of the vibrio now defined as the true cholera vibrio, and the other associated vibrios were thought absolutely unrelated. The following is a summary of the observations made:

V. cholerae could not be isolated from the stools of the general population or from water in the endemic area except in direct relation to the cholera case. Direct close contacts and water in the immediate vicinity showed the presence of *V. cholerae* for short periods only from the onset of a case. The maximum periods of persistence for convalescent carriers, contact carriers and water sources were found to be 13, 9 and 16 days, respectively. 'The cholera case itself would appear to be the major factor in disseminating infection, and close contact carriers and water sources infected from the case may act as intermediaries for short periods and at short range.'

The following factors related to the chemical composition of water and effecting the survival and multiplication of *V. cholerae* in this environmental source were studied to elucidate their possible importance in relation to the endemic prevalence and spread of cholera :

(1) Salt concentration.

(2) Organic matter content.

(3) Hydrogen ion concentration.

(4) The effect of the number of vibrios introduced.

(5) The effect of the presence of other organisms commonly found in water and stools.

The work showed that *V. cholerae* survived longest in saline water at high pH—ur

It was, therefore, of interest to find out whether salt or tidal water areas was in any way related to endemicity. The results of investigation indicated that the conditions in the 'sweet' water areas were apparently more stabilized than in the salt water areas of Bengal. On the other hand, the average total incidence of cholera was higher in the salt water area than in the sweet water area. Observed alterations in the tank water in the tidal area were almost certainly due to changes in the character of the river waters. The reverse was the condition in the sweet water area. Alteration of other factors investigated, e.g. cessation of cholera, increase in the rainfall, fall in the total solids percentage and rise in the total solids chloride ratio in water, and the decrease in agglutinable vibrios followed though with some time lag changes in the system.

On the whole, no constant relationship between the bacteriological and epidemiological findings and the chemical nature of water in these areas could be established. Taylor, however, suggests 'an extension of the investigations to areas of widely different experience of endemic and epidemic incidence may possibly yield information of value'.

Let us now briefly consider some of the other factors with a view to finding out if any of these throws any light on the problem.

(1) Geographical distribution.

In the world, particularly in the Asiatic continent, the endemic areas in general are found peculiarly distributed in coastal areas. It has, therefore, to be seen what meteorological, environmental and other peculiarities are responsible for this selective distribution.

(2) Meteorological and seasonal factors.

Russell and Sundararajan (1928) observed 'climatic factors appear to have no influence whatever on the incidence or spread of cholera.' A preliminary study by Lal and others (1941) of the mean cholera incidence and of seasonal distribution of the disease demonstrates that the districts of Bengal showed heterogeneity as regards their cholera experience, and even different parts of the same district showed considerable heterogeneity. In consequence, smaller units such as thanas were chosen for the tabulation of cholera mortality figures which were then studied in relation to (a) seasonal variation, (b) longer term variations and (c) residual variability by the process of trivariate analysis of variance. The thanas belonged to areas which were classed as endemic or non-endemic according to the following arbitrary criteria:

An area was classed as endemic if during the last 32 years there were not more than 30 months in which cholera deaths were not recorded, and if the maximum period of absence of cholera records was less than 5 months.

This study led to the defining of several areas which showed homogeneous cholera experience. The possible factors concerned,

such as co-variation of cholera mortality with meteorological condition, viz temperature, humidity, rainfall, etc., were studied with allowance for the specific, seasonal and yearly factors associated with the thanas; no significant correlations were established for the areas; the data on the whole threw doubt in Roger's hypothesis of a critical level of absolute humidity (0.4 mm.) affecting the cholera incidence and mortality.

(3) Density of population.

The association between density of population and cholera mortality was studied by the same authors by working out partial correlation co-efficients keeping the area fixed. The correlation co-efficient was insignificant.

(4) Intestinal flora of the population in the endemic area.

No emphasis has so far been laid on the study of this factor. But it has been shown by Linton, Shrivastava and Seal (1938) that the yield of specific substance of *V. cholerae* differs considerably with changes in the constituents of the media. Another fact is that the population all over the areas in the Asiatic continent where cholera is endemic is essentially rice-eating, whereas the Europeans whose diet contains more animal protein do not often suffer from the disease although they may be living for years in these endemic centres where the disease is mostly confined to poorer people. Whether this fact can be explained by the level of sanitary sense is by no means certain.

(5) Changes of vibrio types.

It has been found that vibrio types do not remain constant from year to year or even month by month in any locality in the endemic areas. Inaba is replaced by Ogawa or *vice versa*, or both may be simultaneously present in variable proportions. This has not been adequately explained. The El Tor vibrio has been reported to have caused several outbreaks of cholera in Celebes whereas the association of this vibrio with clinical cholera has been denied by some workers in India although it has been isolated both from human beings and water sources.

(6) Does the endemic strain differ from the epidemic strain?

The phenomenon of variation of virulence is perhaps not doubted, though it is difficult to adduce experimental evidence for want of truly susceptible animals. Lal compared the rate of spread of infection from cases to contacts and he suggested that the epidemic cases show a higher rate of dissemination among the contacts than the sporadic cases. Doorenbos actually classifies the vibrios as 'epidemic strains' and 'endemic strains.' But there is no serological or biochemical means of differentiating these strains.

In view of the above findings, it is difficult to explain sporadic cases in the endemic areas occurring sometimes at interval of months. In other words, the problem of endemicity of

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cholera still remains unsolved. General Sir John Taylor's views on this point may also be quoted:

'Although these facts (as summarized in his review) have been established on the basis of an improved technique and on a sound serological method for the recognition of *V. cholerae*, it cannot be stated that the factors concerned in the production of endemicity of cholera in the area under study have been elucidated. Finality cannot be claimed for the results of one investigation of this nature and the technique used may not have been able to detect a low level of infection in stools and water.'

It will thus be seen that the problem of primary importance in the epidemiology of cholera is the mystery involved in its endemicity. Since the attempt to unravel that mystery on the basis of the hypothesis that the cholera vibrio should exist only in one form has failed, it would perhaps be worth while to reconsider the problem from a different point of view, e.g. the question of variation of the cholera vibrio. The El Tor vibrio differs from the true cholera vibrio only in the matter of hæmolysis; it has been isolated in India both from water sources and healthy individuals. The question also remains whether any change or changes are involved in the existence of the Inaba, Ogawa and intermediate forms just as we have in the three diphtheria forms, viz. gravis, mitis and intermediate. The significance of the finding of lipoid-polysaccharide complex by Linton, Shrivastava, Seal and Mookerji (1938) in the strains collected at the height of an epidemic and the loss of lipoid from the structure at the end of the epidemic has not been fully understood and requires to be followed up. In fact, the important points in this connection which still await answering are:—

(1) Where and how does the cholera vibrio exist before a case occurs in the endemic area?

(2) Does any vibrio, El Tor or any type other than the true cholera vibrio, as defined (Gardner and Venkatraman, O sub-group I) play any part in the endemicity of cholera by its existence in human beings and water sources?

It is quite possible that multiple factors are involved and some of these may be:

(a) Certain peculiarities of the environmental conditions including climate, soil, water, etc.

(b) Intestinal flora of the individual or individuals concerned.

(c) Changes in the vibrio forms in cases, contacts, carriers and water sources.

Thus there are many grounds for further investigation the necessity of which has probably been sufficiently indicated and emphasized in the above discussion.

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Current Topics

Transmission of Sandfly Fever Virus by Sandflies Hatched from Eggs Laid by Infected Females

(Abstract in *Tropical Diseases Bulletin*, Vol. 41, July 1944, p. 565 from the *Med. Parasit. and Parasitic Dis.*, Moscow, Vol. VI, 1937, p. 922)

From the available data it is evident that the virus of sandfly fever is not retained in the human body during the interepidemic period and, therefore, the source of each outbreak of the disease must be sought elsewhere. Whittingham and Rook believed that the sandfly larvæ became infected by ingestion of the faeces or dead bodies of females, and that a newly-hatched imago was incapable of transmitting the infection until it had its first blood meal, which activated the virus. Since these views did not afford a satisfactory explanation, the authors carried out a series of experiments to determine whether the virus is transmitted to the offspring of *Phlebotomus papatasi*

through the ova. Female sandflies (15,331 divided into 47 batches) were fed on patients during the infective period of the disease (not later than 20 hours after the onset of fever), and 2 to 3 days later they were allowed to have another meal on the patients. Those that survived to the 6th to 7th day were fed for the third time. By transferring the insects to new receptacles and collecting the eggs found in these it was possible to determine the time when they were laid. The offspring of the females fed in the endemic area were transported to Moscow for the final tests. The presence of virus in the new generation was determined both for the larvæ and the adults. In the former case, 200 larvæ hatched from eggs laid six days after the first feed of the females, were washed in sterile Ringer solution and then emulsified. The emulsion was injected subcutaneously into two volunteers but produced inconclusive results.

As regards the adult female sandflies these were allowed to feed on 24 volunteers. Thirteen of these were bitten by insects hatched from eggs which had been laid one to five days after the infecting feed of

the parent sandflies. None of these persons showed any evidence of infection, direct or indirect (inoculation of their serum). The remaining eleven volunteers were bitten by sandflies derived from eggs, some of which were laid between the 6th and 8th day after the infecting feed of their mothers. While in six persons of this group there was no reaction, five others showed the typical clinical manifestations of sandfly fever which developed after an incubation period characteristic of this disease. Inoculation of other volunteers with the blood of these patients, taken at the beginning of the pyrexial period, also produced infection.

These experiments have demonstrated: (1) the trans-ovular transmission of the virus of sandfly fever to the offspring of sandflies; (2) that the infection is transmitted to man by the bite of those females of the second generation which had hatched from eggs laid by the parent-insect 6 to 8 days after the infecting feed.

In one of the positive experiments infection was produced by the bites of newly-hatched sandflies, showing that the virus in these insects is transmissible without activation by a previous blood meal.

Sterility

By F. A. BELLINGHAM

(Abstracted from *The Medical Journal of Australia*, Vol. I, 10th February, 1945, p. 129)

TREATMENT OF MALE STERILITY

THE effectiveness of any treatment of male sterility must be controlled by repeated semen analyses. General hygienic and dietary measures should include especially the exhibition of vitamin-B complex and vitamin E. These vitamins seem to have an effect on spermatogenesis. Adequate rest and recreation should be provided with a holiday when necessary. I am sure that overwork and undue fatigue produce many a poor specimen of semen. Iron is necessary in the case of anaemia. Thyroid extract is given partly empirically, but would seem sometimes to improve spermatogenesis. Excessive coitus should be avoided. I have had some successes in cases in which coitus was limited, as far as practicable, to the twelfth to fourteenth days of the wife's menstrual cycle—that is, to the approximate time of ovulation.

GONADOTROPIC HORMONES

My practical experience of gonadotropic hormones is with 'Serogan' and 'Antuitrin S'. The former I have found to give the best results, as it directly stimulates the germinal epithelium of the testis, leading to more active spermatogenesis. Two hundred units of 'Serogan' are given twice a week for six weeks; after a month's rest this course is repeated. Morphological examination then reveals improvement in many specimens. 'Antuitrin S' is mainly used as a prophylactic in younger patients with undescended testes—a condition which greatly lowers spermatogenesis.

ANDROGENIC HORMONES

Androgenic hormones are especially useful when impotence or infrequent coitus are factors. The administration of all hormones would best be scientifically correlated with assays of excretion of gonadotropic hormone.

DYSKYESIS

In my opinion many cases of spontaneous miscarriage are due to subfertile semen, which is adequate for conception, but not for the normal development of the ovum. Probably this is due to deficient excretion of chorionic hormone. Consequently all pregnancies resulting from semen known to be 'below par' should be safeguarded by prophylactic therapy up to four months. I have found 'Antuitrin S (Forte)', one cubic centimetre (500 units) being given twice a week, the most successful injection, together with the exhibition of vitamin E.

Ps. Pyocyanea Meningitis

(From the *Lancet*, i, 27th January, 1945, p. 121)

Most bacteriologists are familiar with the specimen of cerebro-spinal fluid which, particularly if there has been delay in transit from hospital to laboratory, looks a little opalescent but is found to contain nothing abnormal except a pleomorphic gram-negative bacillus which is blithely reported as a contaminant. The frequency of such contaminations was illustrated by Smith and Smith in their isolation of 'coliform' bacilli, white staphylococci, diphtheroids, and non-haemolytic streptococci in 40 per cent of 223 specimens of cerebro-spinal fluid. About a third of these contaminants were judged to come from the water used to rinse and immerse the sterile syringes and needles before spinal puncture. Such contaminating bacteria, apart from being an annoyance and sometimes a snare for the bacteriologist, probably do little or no harm where lumbar puncture is performed for the withdrawal of cerebro-spinal fluid. It is altogether different if fluid is being injected intrathecally, as is done on a considerable scale with anaesthetics and lately with penicillin. Thus Barrie reported 11 cases of low-grade meningitis with one death among 96 consecutive patients operated on under spinal anaesthesia. In that instance a defective filter used for the preparation of sterile water was probably to blame. Now in this issue Frankis Evans reports 2 fatal cases of *Ps. pyocyanea* meningitis following spinal anaesthesia. The source of the organism was not finally traced, but the needle used for lumbar puncture was stored in spirit, a poor disinfectant, and rinsed with 'sterile' saline before use; and rinsing with so-called sterile saline or water is a likely mode of introducing bacterial contaminants. The practice of storing sterile saline or water in large winchester bottles is still too common in hospitals, and no matter how often these bottles are used, the label 'sterile' or even 'distilled' is accepted by the nursing staff as sufficient security, although it is well known that sterile distilled water is easily contaminated.

On another page Botterell and Magner report 11 cases of *Ps. pyocyanea* meningitis—all but 2 of them fatal—from a Canadian neurosurgical unit. The infection in 2 cases was apparently attributable to the intrathecal injection of prophylactic penicillin. Although great care was taken in the preparation of penicillin solutions in the laboratory, and frequent cultures of dispensed samples were sterile, the dregs of two bottles used in the wards contained *Ps. pyocyanea*. In the remaining 9 cases infection was presumed to have spread from the head wound to the subarachnoid space with which it was in direct or close contact. Infection of the wound with *Ps. pyocyanea* was probably present in 3 cases before admission, and Botterell and Magner deprecate incomplete operative interference, unless it is unavoidable, before the patient is admitted to a special unit. Cerebral tissue, if débridement is complete, is relatively resistant to infection with gram-negative organisms, but 'gram-negative pus' in brain wounds, even when there is free drainage, may be followed by fatal meningitis, and therefore every precaution must be taken to prevent its occurrence. In this Canadian unit the surgical no-touch technique, which in McKissock's experience has proved so successful in preventing infection of head wounds, was adopted, but its faithful practice could not always be guaranteed in the face of overcrowded wards and over-worked nurses, and Botterell and Magner attribute at least 4 of their *pyocyanea* infections to ward cross-infection. The risk of such a happening was greatly reduced when they gave up the local instillation of penicillin by rubber tube in favour of primary closure of the wound by suture with penicillin systematically.

These tragic hospital infections are not isolated occurrences, and their courageous publication should be warning enough.

The Differential Diagnosis of Weariness and Fatigue

(From the *Medical Press and Circular*, Vol. CCXIII, 7th March, 1945, p. 146)

A COMPLAINT of weakness is frequently made to the doctor. It may be described as exhaustion, fatigue, loss of ambition or low vitality. What can the doctor do to determine its cause? The author has compiled data in 300 consecutive patients who complained of weakness, fatigue, or weak spells, and presents an answer to the question.

In 61 patients (20 per cent) the complaint was caused by a physical illness. In 239 (80 per cent) it was apparently not due to a physical illness, but was the result of a nervous state.

Of the 61 patients suffering from a physical illness, in 28 it was possible to make a diagnosis by clinical observation alone. In 20 patients the disease was hidden and the diagnosis could not be made without laboratory tests or roentgenograms were needed to confirm or disclose the diagnosis.

An analysis of the physical illnesses causing weakness and fatigue showed the chronic infections were found in 13 patients—3 pulmonary tuberculosis, 8 non-tuberculous pulmonary infection, 1 urinary, 1 syphilitic. Metabolic disorders were found in 12 patients—8 diabetes and 4 myxoedema. Eight patients suffered from heart disease. Sixteen patients had neurologic disorders—4 myasthenia gravis, 8 narcolepsy, and 3 classified as psychomotor epilepsy. Severe anæmias were found in five patients; nephritis in three. Miscellaneous conditions were found in the remaining four, carcinoma of the lung, vitamin deficiency, recurrent fever, possibly due to Hodgkin's disease, and unclassified low-grade fever.

A larger series of cases would almost certainly include important disorders not present in this group, such as Addison's disease and subacute bacterial endocarditis. Yet this group gives a fair picture of what the doctor may expect to meet when he is consulted by a patient who complains of weakness.

If weakness and fatigue are due to a nervous state, this origin will be suggested by the history of the patient, his behaviour under examination and by the quality of his symptoms.

An analysis of the nervous disorders in the 239 patients showed psychoneuroses in 44, mental depression in six, and benign nervous states in 189 (chronic nervous exhaustion 135 patients, nervous fatigue 54 patients).

From the therapeutic viewpoint it is important to distinguish the true neuroses from what may be called 'benign nervousness'. A neurosis is largely dependent on intrinsic factors, whereas a benign nervous state is largely dependent on extrinsic factors. If the patient with a benign nervous state is assured that the physical examination has discovered no disorder he expresses satisfaction. Whereas the true neurotic in similar circumstances is disappointed. He stresses the seriousness of his complaints and insists that some abnormality must be found to account for them.

It can be seen from the records of these 300 patients that vitamin deficiency, endocrine disorders, blood pressure and weak heart considered by the laity and the medical profession to be common causes of weakness, were actually found to be rare, and that weakness due to liver trouble, poor elimination or low blood-pressure was not encountered.

'Found Dead', 'Dead in Bed', and 'Collapsed and Died'.

By J. B. CLELAND

(Abstracted from *The Medical Journal of Australia*, Vol. I, 3rd March, 1945, p. 221)

DURING the last three years, having carried out 100 post-mortem examinations on persons found dead or

having collapsed and died before reaching hospital, I have analysed these cases from the point of view of ascertaining what are the most likely causes of such deaths. Twenty-eight persons were found dead other than in their beds, 20 were found dead in bed, and 52 had collapsed and died before their arrival at the hospital.

As might have been expected, it is seen that coronary atheroma and its consequences were responsible for 40 per cent of these deaths. Nearly half of those who collapsed and died, died from this cause; but it did not play such a prominent part in the case of those found dead. Nine persons died from hypertrophied hearts which had failed. In six subjects very little was found except some dilatation of the heart to which death was attributed, no other reasonable cause for the death suggesting itself. A man, aged fifty-seven years, found dead in bed, had considerable fragmentation of the heart muscle (whatever significance this may have), with slight blood infiltration, very little atheroma in the coronaries and a slightly enlarged and dilated heart (weight 14 ounces or 397 grammes). Four of the patients had valvular disease of the heart, and one died from transverse rupture of the ascending aorta.

There were 15 examples of hæmorrhage within the cranium. Five instances of cerebral hæmorrhage were in persons found dead; two pontine hæmorrhages and a cerebellar hæmorrhage were found in persons who had collapsed and died. Pia-arachnoid hæmorrhage, usually from a ruptured berry aneurysm, was found seven times, four times in patients who had collapsed and died, once in a patient found dead, and twice in subjects found dead in bed. In two additional cases an epidural or subdural hæmorrhage was found at the autopsy to be due to an injury which had occurred some days previously. One patient collapsed and died of meningitis on his way to hospital, as did a subject suffering from lobar pneumonia. There were two other examples of pneumonia or abscesses of the lung and one of acute pulmonary oedema. A woman, aged thirty-five years, and about three months pregnant, was found dead in her doorway from massive pulmonary embolism. A man, aged fifty-seven years, was found dying in his bed, which was saturated with blood that had come from a bleeding duodenal ulcer, the intestines being full of blood which had escaped by the anus. One patient died from a ruptured gastric ulcer and another from a ruptured duodenal ulcer. An alcoholic with a cirrhotic liver was found dead. Alcoholism seemed the principal cause of death of four subjects, two who were found dead and two found dead in bed; in the case of one of these, death may have been due to inhalation of vomitus; in another case the alcohol content of the blood taken at the post-mortem examination was very high, namely, 0.44 per cent (in urine, 0.58 per cent). One death was attributed to heat stroke. In two subjects, one found dead and one found dead in bed, the condition of the kidneys seemed to indicate that death had been due to uræmia.

Of the eight persons with coronary disease out of the 28 found dead, a male, aged seventy-seven years, had infarction of the heart muscle, and six males (aged fifty-two to eighty-three years) and one woman (aged sixty-four years) had coronary atheroma, often with some fibrosis of the heart muscle.

'Sterile Pyuria'

(From the *Medical Press and Circular*, Vol. CCXIII, 7th March, 1945, p. 147)

IN recent years a small but important group of pyurias has been recognized where no evidence of any underlying lesion can be discovered, where careful and repeated search for bacteria in the urine is negative and where cultures on all types of media remain sterile. This condition (referred to as 'sterile', 'abacterial' or 'amicrobic' pyuria), has now been generally accepted as a definite clinical entity.

The aetiology is obscure and the various possible causes (bacteria, toxins, syphilis fungus and virus-infection) have been carefully discussed by Moore in a recent paper, the author himself being of opinion that an ultra-microscopic virus is the most likely underlying factor.

Briggs, on the other hand, believes that a gram-positive coccus is the offending organism in all cases and states that bacteria of this type sometimes appear in the urine after one or more doses of an arsenical.

The symptomatology is often identical with that of urinary tuberculosis and, in cases where a search for tubercle bacilli in the urine has been negative, a meticulous urinary investigation may still leave the observer in doubt as to the true nature of the disease. Under these circumstances a trial course of arsenic may promptly settle a difficult diagnostic problem, as the majority of cases of true abacterial pyuria respond dramatically to this form of treatment.

In view of the danger of untoward reactions in patients whose powers of resistance are often impaired, a smaller dosage should be employed than that commonly used in the treatment of syphilis. It is advisable to start with an intravenous injection of 0.1 g. of novarsenobenzol. This is increased to 0.3 g. over three-day intervals, the total amount given in a course not exceeding 1.2 g.

Condylomata Acuminata

(From the *Medical Press and Circular*, Vol. CCXIII, 7th March, 1945, p. 147)

CONDYLOMATA acuminata may occur in many situations such as the penis, labia, vagina or urethral meatus and are often given the misnomer 'Venereal Warts'. Culp and Kaplan of Texas have found that podophyllin is unusually successful in producing prompt and complete disappearance of condylomata acuminata regardless of size, number, location or duration of growths. The drug is best applied as a 25 per cent suspension in mineral oil. Anaesthesia and hospitalization are not necessary. There is minimal time lost from any type of physical activity.

Most lesions disappear within four days after a single application of the drug. Growths within the urethra usually require two or more treatments.

No ulceration or scarring results and the surrounding normal tissue usually is unaffected by the drug.

Signs and Symptoms of Impending Cerebral Hæmorrhage

By R. D. TAYLOR

and

I. H. PAGE

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXVII, 17th February, 1945, p. 384)

THE records of 40 patients who died with essential hypertension were examined to determine whether or not the clinical courses of those who died of cerebral hæmorrhage were similar enough to allow an accurate prediction of apoplexy. Among this group 19 had fatal cerebral hæmorrhages. Five signs and symptoms were consistently observed. These were: (1) severe occipital or nuchal headaches, (2) vertigo or syncope, (3) motor or sensory neurologic disturbances, (4) nosebleeds, and (5) retinal hæmorrhages in the absence of papilloedema or exudates. These findings were negligible or absent among those patients who died of other causes. It is concluded that demonstration of any four of these manifestations in persons with essential hypertension warrants the assumption that death from cerebral hæmorrhage will occur within 0.8 to five years (average 2.1 years).

Treatment of Infective Hepatitis

(Abstracted from the *British Medical Journal*, i, 24th March, 1945, p. 415)

THE present number of the *Journal* containing details of therapeutic trials of methionine in infective hepatitis by groups of workers at Cambridge and Oxford. In these two series there were 68 treated cases and 68 controls. The conclusion is reached that treatment with methionine has no significant effect on the severity or duration of infective hepatitis or the incidence of relapses.

What are the indications for treatment in infective hepatitis? The first is rest in bed, which should be continued until the liver is no longer tender and the urine is free from bile, preferably by the delicate Hunter reaction. The routine diet should be high in carbohydrate, low in fat, and high in proteins. The emphasis should be on the carbohydrate, and fat should not be reduced to a level at which the food becomes dry and unpalatable. Palatability of the diet and avoidance of undernutrition are indeed primary factors in the treatment of a disease in which loss of appetite is the leading symptom, and Turner came to the sobering conclusion that patients who were allowed to choose their own diet did at least as well as, and in some instances perhaps better than, the average. Fresh milk is often well taken; the cream which separates on standing can be removed, though this is not absolutely necessary. Dried milk is often rejected. Fruit drink ensure a large intake of fluid, carbohydrate and vitamin C. Regularity and frequency of food intake are probably of greater importance than exactness in the composition of the diet, and Turner believes that if patients were given an infusion of glucose for each meal avoided or vomited some disasters might be obviated. Routine treatment with dextrose and insulin, however, is of no advantage, and the same appears to be true of extra vitamins, calcium salts, and liver extract. There is a suggestion that, both liver extract and plasma may produce unpleasant reactions.

Ætiology of Infective Hepatitis

(Abstracted from the *Lancet*, i, 17th February, 1945, p. 213)

THIS week we publish a paper in which Major Havens of the Medical Corps of the U.S. Army, Professor Paul of Yale University, and Major van Rooyen describe transmission experiments made in the United States with materials obtained in 1943 from infected American and British troops in the Middle East. The presence of an infective agent in faeces, inoculable by feeding in gelatin capsules, was clearly demonstrated. Summarizing the results of their own experimental work and that of others, the authors conclude that the virus or infective agent is in the faeces and that the disease can be reproduced by feeding such material or by spraying into the nose and pharynx. They show also that it is reproduced by feeding serum from cases, and point out that the incubation period in this type of experiment is about 28 days—i.e. shorter than the period in 'serum jaundice'. A preliminary communication on p. 212 from Brigadier Findlay and Major Willcox, reporting further experiments on hepatitis, carried out in West Africa, indicates that the causal agent is present in both faeces and urine, and in the faeces in a filtrable form.

Thus we now have a fairly definite picture of the aetiology of epidemic jaundice, confirming ideas dating back to 1915. The infection is a specific one; the causative agent, probably a filtrable virus, invades the body through the alimentary tract, is present in the intestinal contents and in the blood, is discharged in the faeces and possibly also in the urine, and can be transmitted by materials contaminated from an excretal source or by flies. Much work remains to be

done before the virus and its special characters are fully defined; and, as mentioned above, the failure generally to transmit the infection to animals is an obstacle to isolation and study of the virus, and prevents the practical applications that might result from its isolation. The important problem of 'serum jaundice' and its relation to the epidemic disease is one that calls for further examination, as does the associated problem of unrecognized carriers or latent cases of infection.

Cysticercosis (*Tænia solium*) A Further Ten Years' Clinical Study. Covering 284 Cases

By H. B. F. DIXON

and

W. H. HARGREAVES

(Abstracted from the *Quarterly Journal of Medicine*,
Vol. XIII, October 1944, p. 107)

SUMMARY

1. A CLINICAL study of 284 cases of cysticercosis during the past 10 years has brought to light various points of interest.

2. Auto-infestation seems to be a common occurrence, judging from the fact that 26 per cent of patients gave a history of tapeworm infestation. A tapeworm may be harboured unnoticed for years.

3. We have described again the great variety of symptoms which may occur. Severe mental deterioration is unusual, but changes in personality and disorders of behaviour may occur with or without fits. In the case of a soldier who has served in India and whose records show that he has been an efficient soldier the occurrence of such symptoms should arouse suspicion. He should not be labelled with a purely psychiatric diagnosis until the possibility of cysticercosis has been excluded.

4. The diagnosis is not always straightforward. There may be no detectable cysts and no calcification demonstrable radiographically. The history is of first importance. Of our cases 274 were undoubtedly infested in India. It is noteworthy that two had never been outside the British Isles. Only nine were female. Five were children when infested. The stations in India where infestation has occurred most commonly have been enumerated and attention has been drawn to rank, regimental, and occupational incidence.

5. A man who has served in India and gives a suggestive history might well be given the benefit of the doubt, in spite of repeatedly negative clinical and radiographic investigations. An exploratory operation on the brain should not be necessary to prove his case in order that he should be granted a pension. As regards the curative value of neurosurgery, it must be stressed that although the cerebral symptoms may be purely local in character there are, as a rule, multiple cysts in the brain. In none of our cases where the cysticerci have been removed from the brain has the fits been relieved. We consider that the only indication for surgery is threatened blindness from gross papilloedema which calls for decompression.

6. Calcified cerebral cysticerci are not unusual, being reported in 11 per cent of the series, and we are convinced that more would be detected if higher penetration were employed. Their typical radiographic appearances are described and illustrations are given proving that MacArthur's conceptions are correct.

7. The incubation period between infestation of the body and the occurrence of symptoms has been found to vary from a few months to some 20 years.

8. Lastly, we have shown that the prognosis in cysticercosis is considerably better than has been believed.

Too Much Rest

(Abstracted from the *Lancet*, ii, 16th December, 1944,
p. 790)

THE healing power of rest has been acclaimed since Hippocrates. Every doctor can recall patients who owed their recovery to the rest, physical, mental, and emotional, that he brought to the pain-wracked body. Yet like all good things one can have too much of it. In traumatic surgery its limitations have been increasingly recognized—immobilize the fractured bone completely till union is sound, but actively mobilize every joint which does not need to be fixed, is becoming the accepted principle. And a similar principle is beginning to be applied to general surgery. Riddoch, for instance, has protested against the long rest in bed after straightforward hernia operations or laparotomy, quoting the case of a house surgeon who walked upstairs to her room unaided on the third day after appendicectomy, and Hill has adopted a maximum of 10 days in bed for Service men after simple excision of a hernial sac. Powers allows his patients to get up the day after major abdominal operations, and in 100 consecutive cases saw no harm therefrom and a reduced period of convalescence. Eastman of Baltimore supports the views of his colleague Rotstein, that no harm is done by getting a mother up on the fourth day after delivery—in fact, that this early rising encourages involution, stimulates the lochial flow, reduces the incidence of thrombo-phlebitis, and leaves no higher a proportion of retroversions than the traditional ten days. Menninger has little difficulty in demonstrating that the prescribing of rest in psychiatric and psychological disturbances is irrational, and that the restless patient does not need rest alone but the canalization of his energies into channels where they will find their legitimate and satisfying outlet.

It is perhaps in the treatment of heart disease that there is the greatest tendency to over-enthusiastic prescribing of absolute rest. In the American symposium, Harrison quoted experimental work on rats to support his clinical impression that there is seldom any need to keep patients with heart failure or coronary thrombosis in bed for the long periods usually recommended, and he emphasized the liability of bedridden patients to venous thrombosis and the development of a cardiac neurosis. The risk of embolism was stressed by Dock and Levine has urged that recumbency may upset the balance between the right and left sides of the heart and thus increase the strain on the failing heart, besides increasing the total blood volume. In coronary thrombosis we must be prepared occasionally to relax our insistence on absolute rest. Until the third week of the illness absolute rest must practically always be insisted on, to ensure that only the minimum of strain is put on the myocardial infarct until healing is well established. Even in the mildest cases this is a wise rule, the only possible exception being the elderly patient. Subsequently it may be well in some cases not to insist on the patient staying in bed for the usual six weeks. The care of the aged comes into a category by itself. Here it has long been recognized that absolute rest is seldom wise. Even when the heart is obviously failing the old patient is often much better (and happier) sitting in a comfortable armchair than lying in bed. It is regrettable that we seldom see nowadays those large armchairs with a cushioned ledge fixed to the armpieces which used to be a constant feature of all medical wards, and in which the aged patient with a failing heart spent the greater part of his days and nights. Attention to two points will sometimes alleviate the discomforts of rest in bed. One is the use of a bedside commode rather than a bedpan; the other is massage to the legs. Every patient confined to bed, who is not suffering from an acute infection, should have daily massage to the lower limbs, unless there is any lesion in the limbs themselves. Such massage reduces the risk of thrombus formation, helps to maintain the peripheral circulation, and ensures that the muscles do not become atrophied from disuse.

Use of Penicillin for Gonorrhœa Resistant to Sulphonamide Compounds: Report of Four Hundred and Fifty Cases

By L. W. RIBA
C. J. SCHMIDLAPP
and
N. L. BOSWORTH

(From the *War Medicine*, Vol. VI, August 1944, p. 72.
As abstracted in the *Bulletin of Hygiene*, Vol. XX,
February 1945, p. 79)

EACH patient had taken an average total dose of 85 gm. of sulphonamide drugs with no sign of clinical or bacteriological cure. The vast majority showed complications including no less than 302 cases of prostatitis, 58 of urethral stricture, and 33 of epididymitis. It is interesting to note that 71 men had signs of congenital narrowing of the meatus.

The patients were treated according to three different schemes, the results of which may be summarized as shown in table below :—

Number of patients	Penicillin dosage	Total dosage	Failures	REMARKS
112	10,000 units hourly.	100,000 units	11 (9.8 per cent)	6 failures were cured with 160,000 units.
233	10,000 units 3-hourly.	50,000 units	55 (23.6 per cent)	48 failures cured with 100,000 and 1 with 160,000 units.
105	10,000 units 3-hourly.	160,000 units	2 (2 per cent)	1 failure cured with 1,000,000 units.

Five more were cured by re-treatment either with hyperpyrexia plus 100,000 units of penicillin, or with 1,000,000 units of penicillin.

The follow-up period is not stated, but in no case does it appear to have been less than 56 days, during which time the patients were carefully observed and many cultural examinations were made.

The authors believe that penicillin is bacteriostatic rather than bactericidal and that it is particularly important for patients to be observed during the second week after treatment, as it is during that time that the organisms tend to recover from the drug's attending action. Failures can be missed if observation is carried out for a few days only. There was a comparatively high incidence of positive and doubtful smears; the highest incidence of positive smears (21 per cent) occurred between the 7th and 14th days in the group treated with 50,000 units but it was considered that only definitely positive smears and cultures indicated that ultimate failure was likely.

In no case was prostatic massage necessary and the authors have shown that 61 out of 68 initial failures were cured after more penicillin. They conclude that 160,000 units approaches the optimum total dosage of penicillin for the treatment of resistant gonococcal infections in the male, but that the amount of each dose and the intervals between injections need further investigation. Intensive penicillin treatment was sometimes found to be helpful when the usual dosage failed, and some cases of severe gonococcal arthritis were successfully treated intramuscularly and locally with 250,000 or more units.

It is interesting to note that in two obstinate cases *Trichomonas vaginalis* was found to be a secondary invader and that the urethritis in each case cleared after sulphapyridine chemotherapy.

Medical Treatment of Ulcer Hæmorrhage

By C. J. TIDMARSH

(Abstracted from the *Canadian Medical Association Journal*, Vol. LII, January 1945, p. 21)

Prior to the introduction of the prompt feeding regimen, the generally accepted method of medical

treatment consisted of immobilization, starvation and morphine. Immobilization was considered necessary to help control the bleeding, starvation to prevent dislodgment of the clot and morphine to allay restlessness. The treatment was given during and for several days after the hæmorrhage. With this regimen, the mortality rates reported varied from 8.7 to 25 per cent, the majority being in the higher figures.

THE PROMPT FEEDING REGIMEN

In 1927, Andresen recommended the administration of a mixture of gelatin, orange or grape juice and lactose immediately bleeding had ceased, but presented no results. Thus the credit for the introduction of the prompt feeding regimen for ulcer hæmorrhage goes to Meulengracht, who in 1933 reported a series of 109 cases with a mortality of only 1.8 per cent. Starting immediately with the onset of hæmorrhage, he gave his patients a full well-balanced diet, six meals per day, consisting of milk, cereals, eggs, meat, cheese, puréed vegetables, bread, stewed fruits, tea and cocoa. Alkalis and iron were also given.

There have been some reports unfavourable to the Meulengracht regimen. Boyd and Schlackman and others found some patients who could not take the diet at all. Bockus in his recent book on Gastro-enterology argues: (1) that only 30 per cent of Meulengracht's cases had x-ray evidence of ulcer, the majority therefore being cases of erosion or superficial ulcerations; (2) that the ingestion of heavy meals defeats the principle of ulcer management namely acid neutralization and gastric motor rest; (3) that he can see no reason why ulcers which bleed should be treated in such a radically different way from ordinary active ulcers; (4) that 'clinicians inexperienced in ulcer management and incapable of an accurate and rapid estimate of the *status quo* of the hæmorrhage may employ the regimen routinely' with resulting harm in some cases.

MODIFIED REGIMEN ACCEPTABLE

It would seem that as in most arguments the truth lies somewhere between the two extremes, the Meulengracht regimen and the old starvation programme. The principle of prompt feeding has been generally accepted and Meulengracht himself in later papers stated that it didn't matter what the particular diet was provided it was fed promptly. In my own cases, I have used the well-known bland, puréed diet with six feedings at two-hour intervals commenced immediately the patient is seen or admitted. Adequate fluid intake is most important in preventing shock. Morphine and other opiates are avoided in favour of the barbiturates sometimes given subcutaneously but usually by mouth. A mixture containing 1/200 gr. of atropine sulphate and 1/4 gr. of phenobarbitonum per dose given three or four times daily before food has proved to be very helpful as a mild sedative antispasmodic. This is the modified regimen which is proving successful in most clinics on this continent.

TREATMENT OF SHOCK

Immediate therapy is again essential. There may be some delay in obtaining blood plasma so in the meantime start at once 5 per cent glucose saline intravenously and give it slowly. Unless the red blood

cells have fallen below two million, it is not necessary to transfuse with whole blood. In fact, owing to the possibility of reaction and anuria the former practice of giving immediate blood transfusions to patients with ulcer hemorrhage has now been abandoned. If the patient is in shock, blood plasma should be used as soon as possible. About 500 c.c. of plasma and an equal amount of glucose saline is all that is advisable to give the patient in the first twelve hours. When the patient has recovered from shock, start the frequent feedings immediately.

EMERGENCY SURGERY

Although most physicians are now agreed that in view of the low mortality from medical treatment surgery should not be considered, I still believe that in carefully selected patients whose age, history, and clinical findings suggest continued bleeding from a sclerosed vessel, emergency surgery within the first 24 to 48 hours is a life-saving measure.

A Practical Method for Determination of Blood Volume with the Dye T-1824

By M. I. GREGERSEN

(Abstracted in the *Journal of the American Medical Association*, Vol. CXXVII, 27th January, 1945, p. 222 from the *Journal of Laboratory and Clinical Medicine*, Vol. XXIX, December 1944, p. 1266)

A NUMBER of methods have been devised for determination of blood volume; the dye method of Keith and Rowntree has probably been of the greatest clinical value. The method, however, with the modifications introduced in order to secure greater accuracy, has become elaborate and time consuming and requires expensive equipment. Gregersen has described a new dye method which was recently developed for the armed forces. The new technique is the result of several years' work on various aspects of the dye method and of two years' experience with blood volume measurements in various types of experimental shock in animals and in the study of shock in man. According to Gregersen, the assumptions on which the determinations of blood volume are based have been extensively tested under abnormal as well as normal circulatory conditions and have been confirmed by factual data. From this evidence it is possible to define the limits of the error introduced by simplifying the determination on man and to show that this error is negligible in comparison with the reduction in blood volume observed in shock caused by trauma or hemorrhage. Briefly the method includes the following steps: (1) The plasma concentration of the dye T-1824 is measured with the portable Decade Photometer designed by Nickerson. (2) The total plasma volume is obtained from the dye concentration in a single blood sample drawn ten minutes after the dye injection. (3) The critical and troublesome procedure of measuring out an exact amount of dye at the time of making the determination is eliminated by using ampoules containing a standard amount of dye solution of known concentration. This also eliminates all calculations from the determination of total plasma volume. By reference to a chart the plasma volume is obtained directly from the Decade Photometer reading. The total blood volume is then calculated from the plasma volume and the hematocrit. (4) The hematocrit may be determined with the copper-sulphate-specific gravity method instead of with a high speed centrifuge. With the addition of the latter technique all the equipment is readily portable. This method makes it possible to determine the plasma volume and the total blood volume rapidly and with sufficient accuracy for practical purposes. Since the reduction in blood volume precedes the appearance of the symptoms of shock, it constitutes a valuable prodromal sign. Early determination of blood volume may therefore be useful as a means of predicting

whether or not shock is impending. With this information available, shock can be combated before it develops. Intravenous therapy aims to achieve restoration of the normal volume as well as the normal composition of the blood. The data furnished by the hematocrit and plasma protein measurements may be misleading. Gregersen points out that the danger lies not only in failure to maintain an adequate blood volume but also in the excessive use of plasma and of other blood substitutes, thereby running the risk of inducing heart failure or pulmonary oedema. In these cases a determination of the blood volume provides a reliable guide to therapy.

The Role of Injudicious Endocrine Therapy

In the Delayed Diagnosis of Uterine Cancer

By L. C. SCHEFFEY, S.C.D., M.D.

D. M. FARELL, M.D.

and

G. A. HAHN, M.D.

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXVII, 13th January, 1945, p. 76)

It is unfortunately true that only too often the histories of uterine cancer patients show glaring errors of omission or commission in their primary management. Pelvic examination has often been omitted entirely or inadequately performed. Sometimes postponement has been suggested 'until the bleeding stops'. Patients have even been told not to worry—that the condition is one due merely to 'change of life'—and that an examination can be made 'later on'. Of a score of patients coming into our clinic because of abnormal bleeding, the records show that 15 of them had received oral medication without examination, while 5 had been given either 'electrical treatments' or cauterizations or simply told to use a vaginal douche. Biopsy, curettage or reference to a gynecologist or clinic was never even mentioned. Facts like these are not new; they are well known to the profession at large.

In recent years a new hazard has gradually become evident. The current popularity and ease of administration of glandular preparations has resulted in their indiscriminate and injudicious use in an attempt to control abnormal uterine bleeding. Rapid advances have been made in the preparation and variety of potent endocrine products, both natural and synthetic in character. The use of such products should be based on a sound knowledge of their respective physiologic properties. Adherence to scientific principles, accompanied by honesty of purpose and fineness of judgment, is absolutely essential if good instead of harm is to result from their use.

In no sense do we wish to disparage the possible benefits of carefully controlled endocrine medication. It is quite permissible to attempt to manage the functional bleeding of adolescence and the early reproductive period with endocrine therapy, including thyroid, together with adequate general measures, provided a careful physical survey of these younger women, including pelvic examination, has eliminated organic disease and that logical consideration has likewise been given to the physiologic reasons for using this or that endocrine preparation. Even so, the possibility that such therapy may disturb the delicate endocrine balance of the individual should always be borne in mind.

When abnormal bleeding is present during the late reproductive, menopausal or postmenopausal periods, there is much less justification for prolonged and experimental endocrine therapy. Well recognized radiologic and surgical measures are available in such

cases, not only for the relief of organic pelvic disease, but even for the correction of proved functional bleeding—measures that are surer and far less time consuming than prolonged and often indecisive endocrine therapy.

Attention should also be called to the uterine bleeding that may result from excessive and continued dosage with estrogenic substances primarily prescribed to combat the vasomotor disturbances incident to cessation of periods and the menopause. This type of bleeding is bound to be confusing, for the question immediately arises as to whether this substitution therapy is entirely responsible for the postmenopausal bleeding as an estrogenic 'withdrawal' phenomenon or whether it is due to organic pelvic disease, particularly fundal cancer. Only a diagnostic curettage can settle definitely the problem thus created. Furthermore, the possibility of a carcinogenic effect on the postmenopausal genitalia or breast, particularly where susceptibility or a familial history of cancer exists, and entirely apart from a pre-existing cancer, must also be taken into consideration. For the same reason it would seem inadvisable to administer endocrine therapy for the control of vasomotor symptoms occurring after the use of radium or x-rays for either benign or malignant pelvic conditions.

As a matter of fact, many women exhibit little or no disturbance during the menopausal epoch. Quite a number of those who do complain of disagreeable vasomotor symptoms may be made relatively comfortable by a rational explanation of the physiologic changes responsible for their annoyance, plus appropriate sedation and the reassurance of a negative pelvic examination. Too often, however, the menopausal patient is led to believe that courses of 'injections' continued over a long period of time are essential to her health and happiness. She may even be told to expect disagreeable phenomena with the advent of the 'change of life' and such suggestions may come, not only from her intimates, but from her medical adviser as well.

When, after thoughtful consideration, estrogenic therapy is believed to be essential for the control of distressing menopausal phenomena that do not yield to the measures mentioned, it should be administered in the lowest possible dosage. Furthermore, 'rest periods' of a week or so should be prescribed between courses of therapy, as advocated by Hepp and others. Whenever so-called 'withdrawal bleeding' occurs, its possible significance should be promptly appreciated.

The Use of the Dried Blood Agglutination Test in the Diagnosis of Typhoid Fever

By W. GOETERS

(From the *Zeitschrift für Immunitätsforschung und Experimentelle Therapie*, Vol. CIV, December 1943, p. 437. As abstracted in *Bulletin of Hygiene*, Vol. XIX, September 1944, p. 678)

THE agglutination test with dried blood, which is already used in the diagnosis of typhus, may be used as an aid to the rapid diagnosis of typhoid fever. Three separate drops of blood made with a 2 mm. loop are spread over an area 1 cm. in diameter on a slide, and dried in the air. For the test the three drops are mixed respectively with 0.02 c.c., 0.04 c.c. and 0.08 c.c. of a formol-saline suspension of *Bact. typhosum* sensitive to H and O agglutinins. The drops are observed in a moist chamber at times up to 15 minutes.

Agglutination in the second and third drops was found to correspond to tube agglutination to a titre of 1/100 and 1/200, and is considered to be of diagnostic significance in uninoculated persons with no previous history of enteric fever. A positive result in the first drop only is regarded as a weak reaction demanding further investigation.

The dried blood test was found of value in the rapid differentiation of typhoid and typhus fevers.

Reviews

BOOKS RECEIVED

1. Recent advances in endocrinology. By A. T. Cameron. Fifth edition. 1945. Published by J. and A. Churchill Limited, London. Pp. vii plus 215. Illustrated. Price, 18s.
2. Studies of burns and scalds. *Special report series No. 249, Medical Research Council*. 1944. Published by His Majesty's Stationery Office, London. Pp. 210. Illustrated. Price, 4s.
3. Exercises in human physiology. By Sir Thomas Lewis. Published by Macmillan and Co., Ltd., London. Pp. xiv plus 103, with 8 figures in the text. Price, 3s. 6d.
4. Textbook of gynaecology. By W. Shaw. Fourth edition. 1945. Published by J. and A. Churchill Limited, London. Pp. viii plus 636, with 4 coloured plates and 271 text-figures. Price, 24s.
5. Medicine for nurses. By W. G. Sears. Fourth edition. 1945. Published by Edward Arnold and Company, London. Pp. viii plus 460. Illustrated. Price, 10s.
6. A handbook of gynaecology: for the student and general practitioner. By B. Solomons. Fourth edition. 1944. Published by Baillière, Tindall and Cox, London. Pp. xiv plus 352, with 280 illustrations. Price, 25s.
7. Aids to psychiatry. By W. S. Dawson. Fifth edition. 1944. Baillière, Tindall and Cox, London. Pp. viii plus 306. Price, 6s.
8. Ophthalmic nursing. By M. H. Whiting, O.B.E., etc. Fourth edition. 1945. Published by J. and A. Churchill Limited, London. Pp. x plus 133. Illustrated. Price, 6s. 6d.
9. The students' pocket prescriber and guide to prescription writing. By D. M. Macdonald. Twelfth edition. 1945. Published by E. and S. Livingstone Limited, Edinburgh. Pp. xvi plus 348. Price, 4s. and postage 3d. (home).
10. Textbook of anaesthetics. By R. J. Minnitt and J. Gillies. Sixth edition. 1944. Published by E. and S. Livingstone Limited, Edinburgh. Pp. viii plus 487. Illustrated. Price, 25s. and postage 9d. (home).
11. Illustrations of bandaging and first aid. Compiled by L. Oakes. Third edition. 1944. Published by E. and S. Livingstone Limited, Edinburgh. Pp. vii plus 272. Illustrated with 300 photographs and coloured supplement. Price, 6s. and postage 6d. (home).
12. Recent advances in medicine: clinical laboratory therapeutic. By G. E. Beaumont and E. C. Dodds. Eleventh edition. 1943. Published by J. and A. Churchill Limited, London. Pp. xii plus 412, with 43 illustrations.
13. Pulmonary tuberculosis: A handbook for students and practitioners. By R. Y. Keers and B. G. Rigden. E. and S. Livingstone Limited, Edinburgh. Pp. xii plus 273. Illustrated. Price, 17s. 6d. and postage 7d. (home).
14. A handbook of psychological medicine. (With a chapter on wartime mental disorders.) By A. K. Deb. 1945. Published by U. N. Dhur and Sons, Limited, Calcutta. Pp. viii plus 194. Price, Rs. 5.
15. Handbook of practical bacteriology: A guide to bacteriological laboratory work. By T. J. Mackie and J. E. McCartney. Seventh edition. 1945. Published by E. and S. Livingstone, Limited, Edinburgh. Pp. viii plus 720. Illustrated. Price, 17s. 6d. and postage 7d. (home).
16. Bone grafting in the treatment of fractures. By J. R. Armstrong. 1945. Published by E. and S. Livingstone Limited, Edinburgh. Pp. xii plus 175. Illustrated. Price, 25s. and postage 7d. (home).
17. Clinical atlas of blood diseases. By A. Pinney and S. Wyard. Sixth edition. 1945. J. and A. Churchill, Limited, London. Pp. vii plus 138, with 48 illustrations—45 in colour. Price, 16s.

Abstracts from Reports

THE BRITISH EMPIRE LEPROSY RELIEF ASSOCIATION (INDIAN COUNCIL). ANNUAL REPORT, 1944

This report consists as usual of an introductory section by the chairman, Colonel Cotter, report on the activities carried on directly under the Indian Council, and thirdly report on the activities of the different provincial branches. The chairman's report really summarizes the report as a whole and is here reproduced :

GENERAL

As in the previous few years, the work of the Association during 1944 has been carried on under difficult war conditions. However, speaking generally, the quality and quantity of work have been maintained at a satisfactory level. The chief difficulties have been in connection with the publication of our journal *Leprosy in India*, and with the supply of certain drugs and chemicals. On account of the non-receipt of the foreign literature on leprosy, the production of *Leprosy in India* has become more difficult, because of the paucity of suitable material. The non-availability of chemicals, etc., has interfered with the progress of certain research activities.

The activities of our Association are of two kinds : (a) the work done directly under the Indian Council at the School of Tropical Medicine, Calcutta, and elsewhere, and (b) the activities of the Provincial Branches. The central activities and the activities of the Provincial Branches are reported separately later in this report.

As in the previous year, a special feature of the work during the year has been the help given to the Army. Batches of medical officers deputed from the Army have been trained in the diagnosis and treatment of leprosy. During the year 177 patients were referred from military hospitals to the Leprosy Department of the School of Tropical Medicine for diagnosis, and a diagnosis of leprosy was made in 126 cases.

The Government of C. P. and Berar appointed a Leprosy Committee to review the existing anti-leprosy activities in the province, and to make suggestions for future development of the work on sound lines. Dr. Dharmendra, the Research Worker, and Dr. Santra, the Propaganda Officer of the Association, served on this committee, which has made recommendations in the light of the 'Report on leprosy and its control in India' published by the Central Advisory Board of Health. The most important recommendation of this committee relates to the necessity for organizing village isolation centres for infective cases of leprosy. It has been suggested that such isolation centres should be established in connection with the existing leprosy clinics, and that at these centres leprosy should not be tackled as an isolated problem, but should be linked up with other public health and rural reconstruction work, each centre being organized as a health unit.

On the invitation of the Tehri Garhwal State, Dr. Santra spent two months there, to help the authorities in the organization of anti-leprosy work. He visited the leper colony in the State, carried out surveys in selected villages, trained medical personnel in the diagnosis and treatment of leprosy, and made suggestions for the improvement of the work.

CENTRAL ACTIVITIES

The work done directly by the Indian Council consists of (a) research and teaching work in the School of Tropical Medicine, (b) research work at the Bankura Investigation Centre, (c) leprosy survey and propaganda work by Dr. Santra, and (d) the publication of *Leprosy in India* and other propaganda material, etc.

The research work of the Association has, as usual, been carried out in collaboration with the Endowment Fund of the School of Tropical Medicine, and with the Indian Research Fund Association. The research

activities have included clinical, immunological, therapeutic and epidemiological studies. The detailed account of these activities will be found in part II of this report. A summary of the work is given below :—

Clinical studies.—The long-term study of selected cases of the various types of leprosy has been continued. In a large majority of cases, a classification can be made, and a prognosis given, fairly accurately on clinical findings. There are, however, some cases in which the clinical signs are not typical of either of the two types of the disease, and in these cases it is difficult or impossible to make a classification or prognosis. The study is being pursued with a view to correlating the clinical, histological and immunological findings with the prognosis of the disease in such cases.

Immunological studies.—The study of the protein fractions of the acid-fast bacilli has been continued. This study is being made in the hope that an antigen suitable for work in leprosy may be isolated from cultures of some acid-fast bacilli. The results of the study are promising, but so far it has not been possible to obtain a fraction which will produce results uniformly identical with those produced by lepromin prepared from the leprosy lesions of the patients.

Therapeutic studies.—It is customary to add 4 per cent creosote to the hydnocarpus oil or its esters used for injections in treatment. At present creosote is almost unobtainable in the market, and a study has been made to find suitable substitutes. Last year it was reported that the addition of 1 per cent thymol to the oil was found satisfactory. During this year a trial has been made with iodine, and the addition of $\frac{1}{2}$ per cent of iodine to the oil has been found to be quite satisfactory.

Epidemiological studies.—Dr. Santra has concluded the intensive leprosy surveys of small selected areas in the various provinces of India. The study has confirmed the existence of regional variations in the epidemiological features of leprosy in the different parts of the country. The variations affect the incidence of the disease, and the type-distribution, age-distribution, etc., of the cases.

The observed variations cannot be explained by racial or climatic factors alone since these variations have been found in (a) the people of the same race living in different places, and (b) the people of different races living side by side in the same place.

One factor which appears to have a bearing on the observed variations is the attitude of the people towards leprosy and the presence or absence of a custom of isolation in a community. In areas in which the people are apprehensive about cases of leprosy, and where some sort of isolation is practised, a comparatively high lepromatous rate is associated with a low gross incidence, and a low child rate. On the other hand, in the areas where no isolation is practised, a low lepromatous rate is associated with a high gross incidence, and a high child rate. This would indicate that in areas where there is a traditional custom of isolating persons suffering from leprosy, a known number of lepromatous cases produce a smaller number of secondary cases, than in the areas where there is no such custom. This would naturally result in differences in the epidemiological features of the disease in the two groups of areas.

Re-survey at Bankura Investigation Centre.—A re-survey has just been completed of the area under the Bankura Investigation Centre. The re-survey was undertaken with a view to completing the epidemiological studies in progress there since 1936.

The total population of the area in 1944 does not differ materially from that in 1937, when the original survey was completed.

In 1937 the total number of recorded cases of leprosy was 424, giving an incidence of 4.2 per cent. In 1944 the number of recorded cases was 489, giving an incidence of 4.9 per cent.

Teaching.—The annual Leprosy Training Course was held from 22nd May to 3rd June, 1944, at the School of Tropical Medicine, Calcutta.

- As usual, a course of 8 lecture-demonstrations was given to the D.T.M. and L.T.M. classes at the School. Lecture-demonstrations in leprosy were also given to the medical officers deputed from the Army.

Publications and propaganda.—The propaganda material published by the Association is stocked at, and issued from the Red Cross Depot. This material comprised 1,146 books, 618 leaflets, 1,080 posters, and 192 slides. A new book entitled *Popular Lecture on Leprosy* has been published during the year to accompany the new set of slides recently issued. Another pamphlet entitled *The Truth about Leprosy*, issued by the Madras Provincial Branch, was also added to the publications. The quarterly journal *Leprosy in India* which is a record of the study of leprosy and of leprosy work in India and in other countries continues to be issued from the headquarters of the Indian Council. *The Leprosy Review*, which is published by the British Empire Leprosy Relief Association, London, is also circulated in India.

THE PROVINCIAL ACTIVITIES

The reports of the Provincial Branches are abstracted in part IV of this report. These reports indicate that steady progress is being made in the various provinces. The different activities, such as treatment of cases of leprosy, propaganda, teaching in medical institutions, surveys, etc., have been continued. It is gratifying to note that the important question of isolation of infectious cases of leprosy is receiving increasing attention.

Correspondence

PREVENTION OF SMALLPOX BY VACCINATION AND REVACCINATION

SIR,—In reference to the paper entitled 'Prevention of Smallpox by Vaccination and Revaccination' published in the May 1945 issue of your esteemed journal I beg to further supplement my observations by offering the following hypothesis regarding the conception of immunity and its fluctuations, conferred by smallpox vaccination and revaccination. The hypothesis is based on the observations discussed in the article and is further strengthened by the field experience during the recent outbreak of smallpox in certain rural areas of Bengal.

After primary vaccination the immunity shoots up within 2 to 3 weeks and reaches a certain level which may be defined as 'high' in most instances, and remains at or near that level for varying periods differing according to the individual response (idiosyncrasy), say 2 to 5 years or more, and then declines gradually with a steady fall in certain cases or with regular and irregular fluctuations in others according to the circumstances of health and general resistance and after varying intervals in different individuals, it reaches a critical level. So long as it does not reach this critical level the individual concerned will give only negative reaction on revaccination but it does not probably raise the immunity level, contrary to our experience with the Schick test in diphtheria. When the aforesaid level is crossed in its downward trend the individual becomes liable to react with either a vaccinoid reaction or a primary take according perhaps to the level to which it has fallen below this critical point (i.e., near the border line or clear below the border line). Once the reaction is like a primary take it probably affects the immunity in the same way as in the case of primary vaccination. Further, the immunity response may not be uniformly high in all individuals after primary vaccination as well as in case of primary takes after revaccination; secondly, in certain individuals the immunity conferred by vaccination may remain above the critical level for a very long time while in others it may go down fairly quickly; thirdly, the critical level may have a small range depending upon the potency of the lymph used for revaccination; and lastly individuals giving negative or immune reaction may be at any stage above the critical level and the

degree of safety or risk is subject to modification according to the other epidemiological factors to which an individual is exposed.

Let us re-examine some of the irregular cases already alluded to in terms of the above hypothesis.

1. Cases occurring within a short time (maximum 3 years) of successful revaccination.

The immunity in these cases did not apparently rise very high after the last revaccination and thus it fell below critical level or it was just in the border line when they exposed themselves either to heavy infection or virulent strain and succumbed to the infection.

2. Cases amongst those found refractory to repeated primary vaccination—Campbell Hospital case and New Zealand ship case.

At the time when the primary vaccination was repeatedly tried their immunity (? genetic) was above the critical level for which they showed negative reaction, but their immunity which was not apparently reinforced by this repeated vaccination was temporary and within a short period fell below the critical level when the heavy exposure brought them the infection.

3. Case 10. Glasgow (1942) ship case (age 11 months).

This is an example of a case which proved refractory to primary vaccination and yet suffered from the disease. This child had just enough immunity (border line of critical level) to give negative reaction but when exposed to heavy infection his immunity barrier broke down or it may be a case of false negative reaction due to the absence of tissue response to the virus.

4. Cases amongst those who gave history of repeated revaccination.

This shows that revaccination even if done several times may not give security against infection. It will depend upon whether the revaccination was followed by a primary take or not and at what stage of the curve the individual immunity lies at the time of exposure, the lapse of time after successful revaccination being also an important factor.

5. Occurrence of cases among the negative reactors.

The negative reactors according to the hypothesis are only relatively immune depending upon at what stage of the curve the immunity in the individual lies. Thus border line cases are liable to suffer when heavily exposed or when the immunity level falls below the critical level. In an outbreak a single unsuccessful vaccination should not therefore be accepted as evidence of immunity in the absence of a history of recent successful vaccination.

6. Occurrence of cases among the positive reactors.

It is expected that the immunity against smallpox becomes reinforced after a successful revaccination. But often quite a number of cases have been reported among such individuals as in the Glasgow and other outbreaks including cases in our own experience. This may be explained on the assumption that immunity from successful vaccination was not developing rapidly enough to afford complete protection. While in other cases in which the revaccination was successfully done well ahead of the incubation period there are several possibilities, viz, (1) immunity was not stimulated to a sufficiently high level, (2) it soon fell near or below the critical level, (3) the question of the virus strain.

In all the above cases the other factors, e.g. potency of the vaccine, technique of vaccination, virulence of the strain, quantum of infection, herd immunity and other epidemiological factors should also be simultaneously considered.

I have the honour to be,

Sir,

Your most obedient servant,
S. C. SEAL.

ALL-INDIA INSTITUTE OF
HYGIENE AND PUBLIC HEALTH,
110, CHITTARANJAN AVENUE,
CALCUTTA,
12th June, 1945.

'TORONTO UNIT'

SIR,—I would be grateful if you will be so good as to clear up some confusion in my mind as regards the exact meaning of a 'Toronto unit' as applied to heparin in weight.

I have understood the Toronto unit to stand for that weight of heparin which prevents 1 c.cm. of cat blood from clotting when stored in the cold, the weight being 1 mgm.

In your April 1945 issue of the *Indian Medical Gazette* on page 187 it is stated that one Toronto unit contains 0.01 mgm. of heparin from which it can be deduced that 100 Toronto units equal 1 mgm.

On page 326 of *Recent Advances in Medicine* (1944), the preparation is said to contain 500 units per mgm.

On page 292 of the *Medical Annual* for 1944 it is again stated that 10 c.cm. contains 100 mgm. (manufacturer's name not given). British Drug House puts it up in 10 c.cm. tubes containing 100 Toronto units from which, if read with the immediately foregoing paragraph, it would appear that one Toronto unit equals one mgm.

It is all very confusing and I would be grateful if you will please help.

B. I. BOUCHE, M.R.C.S., L.R.C.P.,
MAJOR, I.M.D. (Retd.).

'WISTERIA',
MUSSOORIE.

[Editorial Note.—Dr. B. Mukerji of the Biochemical Standardization Laboratory replies to this letter as follows :—

'The "Toronto unit" of heparin is 0.01 mg. of the crystalline barium salt of heparin prepared by Charles and Scott (*Biochem. J.*, 30, 1927, 1936). The Health Organization of the League of Nations (Department of Biological Standardization) have now adopted the crystalline sodium salt (not barium salt) of heparin as the "International unit". This preparation contains 130 units per mg., the ratio of the sodium salt to the barium salt being 130 : 100. The term "Toronto unit" is getting gradually replaced in modern scientific literature by the "International unit", though both of these are practically identical in potency.

The reference quoted in the *Recent Advances in Medicine* (1944) was based on an earlier paper (1933), in which the same workers claimed 1 mg. = 500 units heparin. This work has since been superseded.

It would clarify all confusion if Dr. Bouché keeps these two lines recorded in his notebook :

1 mg. = 130 I.U. (previously "Toronto unit") of crystalline sodium salt of heparin.

1 mg. = 100 I.U. of crystalline barium salt of heparin.]

Service Notes

APPOINTMENTS AND TRANSFERS

The services of Colonel G. R. Lynn, C.B.E., D.S.O., I.M.S. (Retd.), Additional Deputy Director-General, Indian Medical Service (Stores), are placed at the disposal of His Excellency the Commander-in-Chief, with effect from the 1st May, 1945.

The services of Colonel S. L. Bhatia, M.C., are placed at the disposal of the Government of Assam, with effect from the 20th May, 1945, for appointment as Inspector-General of Civil Hospitals and Prisons, Assam.

The following officers are appointed as Medical Advisers (Pensions) in the War Department. Dated 1st April, 1945.

Lieutenant-Colonel Hari Das.

Lieutenant-Colonel G. H. Fraser.

Lieutenant-Colonel A. R. Woodforde.

Lieutenant-Colonel F. H. Whyte is appointed Civil Surgeon, Simla West, and Officer-in-Charge, Civil and

Military Dispensary, Simla, with effect from the 19th April, 1945.

Lieutenant-Colonel M. K. Kelavkar, O.B.E., Assistant Director-General, Indian Medical Service (Stores), is appointed as Additional Deputy Director-General, Indian Medical Service (Stores), with effect from the 1st May, 1945, vice Colonel G. R. Lynn, C.B.E., D.S.O., I.M.S. (Retd.), reverted to military employ.

With effect from the same date Major B. A. Porritt, Additional Assistant Director-General, Indian Medical Service (Stores), is appointed as Assistant Director-General, Indian Medical Service (Stores), vice Lieutenant-Colonel M. K. Kelavkar, O.B.E.

Major M. K. Afridi to be consultant and is granted the local rank of Brigadier. Dated 5th August, 1944.

Major E. L. Jones is appointed as Assistant Director-General, Indian Medical Service (Recruitment), with effect from the 1st March, 1945.

Major C. K. Lakshmanan is appointed Director, All-India Institute of Hygiene and Public Health, Calcutta, with effect from the afternoon of the 16th April, 1945.

On the expiry of his leave the services of Major H. P. Lal, Officer Commanding, Civil Defence Hospital Train No. 1, were replaced at the disposal of the Bihar Government, with effect from 16th May, 1945.

Major G. P. Charlewood is appointed Civil Surgeon, Ajmer, with effect from the afternoon of the 2nd June, 1945.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)

To be Captains

Raghubar Chowdhury. Dated 5th February, 1944.

Harish Chandra Paliwall. Dated 19th October, 1944.

Mohammad Zeaul Hasan. Dated 8th December, 1944.

Alfred Saldanha. Dated 2nd February, 1945.

Prem Govinda Saha. Dated 23rd March, 1945.

Cuddalore Tezuvoncadam Gopalkrishna Tilak. Dated 29th March, 1945.

Prakash Nath Ojha. Dated 2nd April, 1945.

Lavu Sivaiah. Dated 3rd April, 1945.

Birendra Kumar Acharyya. Dated 14th April, 1945.

H. Venkatraya Gadiyar. Dated 18th April, 1945.

Dhanjishah Fardunji Mehta. Dated 26th May, 1944.

19th April, 1945

Sudhamay Chakravarty. Falak Sher Khan.

Sukhdev Radhakishin Batheja. Dated 20th April, 1945.

To be Lieutenants

26th November, 1943

Douglas Hammond Niblett.

Terence Albert DeSena.

Roland Mervyn Stanley Terry.

Tarapada Acharyya. Dated 7th March, 1945.

19th March, 1945

Birendra Kumar Basu.

Syed Ataur Rahman.

Bhupati Ranjan Mukherjee.

Muckatira Mandanna Chengappa.

Prem Kumar Mishra.

Shiv Nath Bhandari. Dated 8th April, 1945.

Pabitra Kumar Raychaudhuri. Dated 18th April, 1945.

Solomon Thomas Ohol. Dated 21st April, 1945.

Janeswar Prosad. Dated 23rd April, 1945.

INDIAN MEDICAL SERVICE—SECONDED TO THE INDIAN
ARMY MEDICAL CORPS

(Emergency Commission)

(WOMEN'S BRANCH)

To be Captains

(Miss) Charlotte De Quadros. Dated 12th March, 1943.

(Miss) Siloo Sorabji Daruvala. Dated 15th April, 1943.

(Miss) Winifred Agnes Vaz. Dated 19th April, 1943

(Miss) Khorshed Irani. Dated 20th May, 1943.

(Miss) Sarah Abraham Shellim. Dated 25th September, 1943.

(Miss) Roshan Nusserwanjee Chinoy. Dated 17th January, 1944.

(Miss) Beatrice Mary D'Sousa. Dated 1st August, 1944.

The following officers have been re-transferred to the Army (Indian Army Medical Corps):—

ROYAL INDIAN NAVAL VOLUNTEER RESERVE

1st April, 1945

Temporary Acting Surgeon Commander P. S. Clarke.

Temporary Surgeon Lieutenant-Commander B. P. Srivastava.

The undermentioned officer of the Indian Medical Service (Emergency Commission) reverts from the R. I. N. V. R., and is seconded to the I. A. M. C.:—

Surgeon Lieutenant N. S. Shroff. Dated 15th February, 1945.

PROMOTIONS

Major-General Sir E. W. C. Bradfield, K.C.I.E., O.B.E. (Retd.), is granted the local rank of Lieutenant-General (without effect on pay or pension), while holding his present appointment. Dated 27th October, 1944.

Colonel to be Major-General

D. V. O'Malley, O.B.E., V.H.S. Dated 17th April, 1945.

Major to be Lieutenant-Colonel

C. L. Pasricha. Dated 20th May, 1945.

Captains to be Majors

1st May, 1945

G. R. C. Palmer. T. Sommerville.

J. Revens. A. C. Taylor.

J. G. Thomson.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commission)

Captain to be Major

P. S. Dorai Raja. Dated 13th January, 1945.

Lieutenants to be Captains

26th November, 1944

D. H. Niblett. T. A. D'Sena.

R. M. S. Terry.

5th May, 1945

T. S. Bhaskaran. R. K. Moorthy.

B. L. Shenoy.

G. C. Ambunathan. Dated 6th May, 1945.

8th May, 1945

P. R. Kutty. C. R. Gopinathan.

H. S. Nayak. P. S. B. Naidu.

P. S. Ramachandran. V. P. K. Pandyan.

M. Narayanan.

V. C. Nayanar. Dated 10th May, 1945.

15th May, 1945

S. J. Luxa. A. P. Bedell.

P. B. W. Price. J. E. Ferris.

S. P. Benjamin. Dated 24th May, 1945.

T. P. Banerjee. Dated 25th May, 1945.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(WOMEN'S BRANCH)

(Emergency Commissions)

Lieutenants to be Captains

(Miss) S. Mitra. Dated 18th April, 1945.

(Mrs.) D. E. MacQueen. Dated 23rd April, 1945.

Lieutenants (on probation) to be Captains (on probation) (Relative Rank)

(Miss) P. S. Mavar. Dated 8th April, 1942.

(Miss) F. P. Wadia. Dated 4th May, 1942.

INDIAN MEDICAL SERVICE—SECONDED FOR SERVICE WITH
THE ROYAL INDIAN NAVY

(Emergency Commission)

Lieutenant to be Captain

G. P. Colaco. Dated 9th May, 1945.

RETIREMENTS

Lieutenant-Colonel E. C. A. Smith, 20th August, 1944.
Lieutenant-Colonel P. F. A. Grant, O.B.E., on account of ill health, 16th October, 1944.

Lieutenant-Colonel P. N. Lahiri, 11th May, 1945.

Lieutenant-Colonel B. Basu, O.B.E., 21st May, 1945, and is granted the honorary rank of Colonel.

RESIGNATIONS

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Lieutenant Naranjan Dass Chhibber. Dated 31st March, 1945.

Temporary Major B. C. Chatterjee. Dated 12th June, 1945.

RELINQUISHMENTS

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE

(Emergency Commission)

Captain A. Gray relinquishes his commission on account of ill health. Dated 2nd February, 1944, and is granted the honorary rank of Captain.

Temporary Major Hari Prakash Lal. Dated 16th May, 1945, and is granted the honorary rank of Major.

SECONDED TO THE INDIAN ARMY MEDICAL CORPS

Captain Gandharv Singh Sarin. Dated 9th June, 1945, on grounds of ill health and is granted the honorary rank of Captain.

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Original Articles

CHRONIC ENDEMIC FLUOROSIS
(WITH BONE AFFECTIONS)
IN THE PUNJAB

By KHAN BAHADUR YAR MOHD. KHAN, M.D.
*Professor of Medicine, King Edward Medical College,
Lahore*

and

K. L. WIG, M.B., B.S. (Pb.), M.R.C.P. (Lond.),
M.R.C.S. (Eng.), D.T.M. & H. (Lond.)
*Clinical Assistant to Professor of Medicine, King
Edward Medical College, Lahore*

SINCE the investigation of Black and McKay in 1916 into the problem of mottled enamel, and the definite association of this anomaly with the fluorine content of drinking waters by Churchill (1931, 1932), the matter of fluorine intoxication has been studied in detail by different workers in various parts of the world. It has been shown that this mottling of the enamel occurs only if the fluorine content of the water is above 2 to 3 mg. per litre (Smith and Smith, 1932) or, at any rate, above 1 part per million (Smith *et al.*, 1935).

It has been found by various workers that although the most obvious effect of chronic fluorine intoxication is the characteristic tooth mottling, yet this is only a part of the picture, and the rest of the skeletal tissue and certain other systems also get affected. It is however only rarely and under certain special conditions that clinical affections of the bones and other systems manifest themselves.

Roholm described in 1937 cases of acute and chronic fluorine poisoning contracted by cryolite workers through dust inhalation. The commonest symptoms exhibited by these workers were nausea, vomiting, and various bone, joint and muscle symptoms—the chief of which was stiffness, especially of the spine. Characteristic bone changes were described. Fluorine intoxication of plants and animals also has been observed in close proximity to metal, glass or super-phosphate factories where raw material containing fluorine is used.

The condition of chronic fluorine intoxication, which in most cases has been first recognized through the typical and vivid clinical picture of enamel mottling, is really widely spread throughout the world. It has been reported in 325 districts in 25 states of the United States (Dean, 1937), in Mexico, Argentine, Barbados, and the Bahama Islands. In Europe, it has been recognized in England, Spain, Italy and the Netherlands. In fact, in some parts of England the incidence of mottled enamel seems to be quite high. Spira (1942), examining 5,019 service men and women, found mottled teeth in 1,099 or nearly 22 per cent. The proportion was highest in those who had lived in Hertford-

shire and Northamptonshire. The condition has also been reported from Morocco, Tunisia, Algeria, South Africa, the Azores, Cape Verde Islands, North China and Japan.

In India, so far as bone symptoms are concerned, the first report of the cases was by Shortt, Pandit and Raghavachari (1937), and Shortt *et al.* (1937) who discovered marked skeletal changes with mottled enamel in patients coming from the Nellore District of the Madras Presidency, and, complaining of certain skeletal symptoms notably stiffness of the spine. The diagnosis of fluorine intoxication was made, and later detailed investigations confirmed the diagnosis and proved it to be due to the high content of fluorine in water.

Certain investigations tend to show that sensitivity to fluorine is influenced to some extent by the calcium, phosphorus and vitamin D content of the diet. Phillips (1933) demonstrated a relationship between vitamin C and chronic fluorine intoxication, and certain investigations in Madras (Pandit *et al.*, 1940) also tended to prove that the skeletal changes were more likely to occur if, along with a high fluorine content of water, there was deficiency of vitamin C in the diet.

The main pathological lesion in the teeth generally occurs in those people who have spent the first fourteen years of life in an area with a high fluorine content of water. The teeth lose their glossy translucent appearance and appear chalky white or opaque on the areas which had been affected during calcification, the lesion being due to the absence, to a greater or less degree, of the cementing substance between the enamel. A common manifestation is the appearance of white, yellow, or brown areas in the form of bands extending horizontally across the tooth surface. Sometimes the affected areas are very irregular in outline, and closely resemble 'flow-pattern' porcelain.

Skeletal changes are very rare in comparison with the incidence of mottled enamel. Apart from workers in factories of cryolite, etc., they have been found in certain villages with a very high content of fluorine in water (6 parts per million). There is some evidence to suggest that although dental fluorosis and fluorosis of bones are both primarily due to fluorine poisoning, the mode of action of the causative element in the production of the two conditions may not be identical. Pillai, Rajagopalan and De (1944) have shown in experimental animals that the addition of milk powder or bone powder to their diet affords remarkable protection against fluorine poisoning—especially against the bone symptoms.

The main changes in the skeletal tissues when they are affected as described by Roholm (1937) are:—

The pelvis and the spine are the earliest to be affected. Ultimately the changes affect the ribs, the skull and the bones of the extremities also.

Briefly the bones show diffuse osteosclerosis, and the ligaments and muscular attachments show calcification.

The cortex of the long bones shows a marked thickening, and irregular periosteal new formation of bones may occur, giving rise to the development of palpable nodules. The motility of the spine is markedly diminished, but the restriction of movements in other joints is not so marked.

X-ray appearances are characteristic and diagnostic. They vary with the degree of affection, but in the majority of cases the spine and the pelvis show the most advanced changes. Roholm divides the changes into the following three phases:—

1st phase.—The spinal column and the pelvis are affected. They show the roughening and blurring of the trabeculae.

2nd phase.—The trabeculae merge together and the bone structure is blurred and becomes a diffuse structureless shadow. The bone contours become uneven.

The above changes are marked in the pelvis, spine and the ribs. The extremities are still in the first phase. The medullary cavity is however narrowed, and the ligaments show incipient calcification.

3rd phase.—The bones show the appearance of marble-white shadows, this appearance being most marked in the central bones. Bone contour is woolly. The bones of the extremities show irregular periosteal thickening. There is definite calcification of ligaments and muscle attachments—especially noticeable at the insertions of the intercostal muscles and giving rise to 'rime frost needle' appearance. The cortex of the long bones is dense and thick, and the medullary cavity diminishes. There is no evidence of bone destruction. The x-ray appearances of bones, etc., in cases published by Shortt and his co-workers from Madras were very similar.

As for changes in other tissues, calcification of the walls of blood vessels has also been noted, and Roholm observed fibrosis of the lungs.

Changes in other organs have not been seen in human beings. In animals suffering from fluorine intoxication, Roholm observed nephritis, changes resembling osteomalacia, anaemia, anorexia, and emaciation.

In the Punjab, Day (1940) described in detail a survey of school children done by him for this condition (enamel mottling due to fluorosis) at Kasur nearly 40 miles from Lahore. It was found by him that between the ages of 5 and 18, 100 per cent of the children who had lived in Kasur from the date of birth showed mottling of the enamel to a greater or less degree, varying from slight to severe. According to his observations on patients, the disease is endemic in the Kasur area (Lahore District) and the districts of Ferozepur and Mianwali in the Punjab. He found the fluorine content of water in the various wells in Kasur area (except in one well) to vary from 1.2 to 6.4 mg. per litre—a level which is capable of causing fluorine intoxication—at any rate enamel mottling. He found the fluorine content of a sample of water from a tube-well at Lahore, which town he regards to be a non-endemic area, to be only 0.6 mg. per litre.

Shourie (personal communication) who analysed 129 samples of water from Lahore District, found the fluorine content to vary from 0.2 to 7 parts per million. In a survey of policemen

(18 to 55 years of age) stationed at Lahore but recruited from different areas of the Punjab, he found evidences of fluorine mottling—varying from slight to a severe degree—in policemen recruited from Hissar, Karnal, Ferozepur, Ludhiana, Lahore, Amritsar, Mianwali, Gujrat, Campbellpur, Jhelum and Sialkot districts.

Wilson (1941) found a high degree of dental fluorosis in Hundewali (Punjab), and, according to Day, the Delhi Shahpur Salit range running obliquely across the Punjab through Hissar, Ferozepur, Kasur, Sangla Hill, Chiniot, Hundewali, Sargodha, Shahpur and on to Mianwali District is responsible for the fluorine in well water; hence people living along this range are likely to develop mottling of the enamel.

No case of bone affection due to fluorosis has so far been published from the Punjab or even diagnosed, so far as we are aware, in any of the major institutions of the Punjab. As far as we are aware, apart from the above-mentioned cases from Madras, the bone affections have not so far been noticed in any other part of India.

During the last few years, two cases from the Punjab have come under our observation which were studied by us from all points of view, and about which we came to the conclusion that they resembled in every detail cases of fluorine intoxication described by Roholm in Denmark and in India by Shortt and others in Madras. Very marked mottling of the enamel in these cases supported this view.

The clinical histories and findings of these cases are as follows:—

Case 1

Naginder Singh, a Sikh male agriculturist, aged 25 years, resident of a village in Tahsil Zira, District Ferozepur, was admitted in the Mayo Hospital in November 1941, as a case of severe anaemia and gave the following history:—

Three years ago, he suffered from breathlessness on exertion and about the same time developed a skin rash for which he was given five injections of neosalvarsan. With these he developed frequency of micturition which was followed by generalized anasarca, which lasted for six months and then yielded to some indigenous method of treatment. When the oedema disappeared, he noticed that there was limitation of movements especially marked in the spine, elbows, knees, ankles, and the small joints of the hands and feet.

He again developed generalized oedema in August 1940 and was then admitted into the Mayo Hospital and diagnosed as syphilitic osteo-periostitis and anaemia. He somehow stayed in the hospital for only a few days then, and so no detailed investigations could be done on him.

In November 1941, he sought admission into the hospital again. His physical examination and laboratory investigations revealed the following picture:—

He was markedly pale and anæmic. He showed clubbing of the fingers which he stated was present since infancy. Nearly all the joints were markedly stiff and showed limitation of movements. The ankles were fixed in plantar flexion, and he had to stand and walk on tip-toe. His face showed dark pigmentation, and teeth showed very extensive mottling indicative of fluorosis. The spleen was just palpable on deep inspiration. The liver was palpable two fingers below

the costal margin. The heart showed a hæmic murmur over all the areas, but the systolic murmur over the aortic area was harsh and was conducted up to the outer end of the right clavicle.

The laboratory findings were as follows:—

Hæmoglobin	.. 30 per cent
Red blood cells	.. 1,970,000 per c.mm.
Colour index	.. 0.8
Diameter of red cells	.. 6.99 μ
White blood cells	.. 8,800 per c.mm.
Neutrophils	.. 60 per cent
Lymphocytes	.. 35 per cent
Large mononuclears	.. 5 per cent
Eosinophils	.. Nil
Blood urea	.. 154 mg. per 100 c.cm.
Blood calcium	.. 9.6 mg. per 100 c.cm.
Blood phosphorus	.. 5.02 mg.
Phosphatase	.. 7.4 units
W.R.	.. Negative
Urine	.. Sp. gr. 1008. Albumin present in fair amounts. Granular and hyaline casts present in fair numbers.

Stools showed no abnormality.

Skiagrams of the bone (figures 1-4, plate XIV) showed marked thickening of the cortex, narrowing of the medullary cavity and calcification of ligaments and muscular attachments. Calcification is also seen round about the blood vessels.

There was nothing of importance in the family or the personal history, except as stated above and fracture of one leg some years ago. The diet had always been good and mixed, consisting of milk, bread, vegetables, butter and ghee.

It is obvious that the patient was suffering from a condition of chronic damage to the kidneys. In addition there was a marked degree of microcytic hypochromic anæmia which might be the result of the kidney condition or might have been due to the bone condition. The bone condition seems to us to be the result of fluorosis. In view of his anæmia, the possibility of marble bones (Albers-Schonberg disease) was considered, but the deposits of calcium outside the bones rule that out. He came from an area where the fluorine content of water is known to be very high, and it is possible that the anæmia and especially his kidney condition which meant deficient powers of secretion hastened the onset of the skeletal changes due to fluorosis, as usually this condition is seen at a much later age. The condition of the teeth was obviously one of a marked degree of fluorosis, and supported the diagnosis so far as the skeletal changes were concerned.

Case 2

Kehar Singh, a Sikh male agriculturist, aged 55 years, resident of a village close to Bhatinda in Patiala State, was admitted on 12th June, 1942, with an outpatient diagnosis of anæmia and general anasarca. He gave the following history:—

About ten months previously he had been bitten by a camel over his left forearm, with a resulting fracture. There was a persistent sinus over his wrist joint at the time of examination.

A month after the bite, he developed fever which lasted for about one month. During the course of this fever he developed generalized oedema and progressive weakness. These complaints persisted and became progressive, even after the fever had subsided.

There was, in addition, a complaint of persistent cough and profuse expectoration which was of eight

years' duration and started after an attack of pneumonia. There was also a complaint of pain in both the legs and a feeling of stiffness of the whole body and all the joints of a long but of vague duration.

On physical examination he was obviously anæmic. He was thin and emaciated. The teeth showed an extreme degree of mottling due to fluorosis. The gums showed a mild grade of suppurative periodontitis. The tongue was pale but clean with no evidence of ulceration.

The chest was practically immobile. The note over it was resonant and there were diffuse catarrhal signs more marked at the bases.

Examination of the heart showed no definite abnormality. The abdomen showed evidence of free fluid in the peritoneal cavity, which was tapped. There was no enlargement of the liver or spleen.

There was a moderate degree of oedema over the legs as well as the arms and a general puffiness of the face.

The spine showed a generalized kyphosis. It was extremely rigid and the patient could not straighten himself at all. He seemed to be stiff in all the joints. One of the ribs showed an apparent thickening at one point—as if there had been a previous fracture. Two nodules could be felt over the right tibia and one over the right radius. The patient on questioning gave the information that they were of very long duration.

Laboratory examinations

1. Ascitic fluid was pale yellow, clear, specific gravity 1010, albumin in fair quantities (quantitative examination was not done); microscopically there were only a few cells.

Blood.—Hb.—30 per cent, total R.B.C.—1,530,000, colour index—I, diameter of red cells (Halometer reading)—7.6 μ , total W.B.C. count—3,200, neutrophils—68 per cent, lymphocytes—30 per cent, large mononuclears—2 per cent, eosinophils—0.0 per cent. W.R. was negative. Serum calcium—8.5 mg. per 100 c.cm. Phosphorus—3.9 mg. per 100 c.cm. Phosphatase—6.1 units (Bodansky).

Urine.—Showed no abnormality on chemical or microscopic examination. Sputum showed no tubercle bacilli. A skiagram of the chest revealed a peculiar condition of the ribs, and in view of this as well the symptoms of rigidity and stiffness, skiagrams of different parts of the skeleton were taken (see plates XIV and XV). All of them revealed a characteristic condition (figures 5-8)—marked thickening and increased density of the cortex of the bones. In addition, outside the bones in the muscles and ligaments and in one skiagram round a blood vessel, deposits of calcium could be seen. One of the ribs showed an old fracture; as there was no history of injury it must have been spontaneous.

Previous history revealed nothing of importance. He had always lived on a poor quality diet—consisting of wheat, bread and some *dal*, with practically no meat and no vegetables. He hardly ever took any milk but could get *lassi* very occasionally.

With the treatment of his condition by a proper diet, iron and liver extract, the anæmia improved. Oedema became less and there was an improved feeling of well-being, but his stiffness and general weakness persisted.

The blood picture at the end of July was: Hb.—35 per cent, total red cell count—2,370,000, colour index—0.75, total W.B.C.—7,400, neutrophils—54 per cent, lymphocytes—36 per cent, large mononuclears—8 per cent, eosinophils—2 per cent.

The anæmia was of the normocytic type and was probably of nutritional origin; no other cause at any rate could be detected. In view of the absence of any evidence of cardiac failure, and of negative findings in the urine, the oedema was in all probability the result of his anæmia and other nutritional factors.

The condition of the bones could not be ascribed to the above factors—though anæmia may possibly be the result of the bone condition. In our opinion the x-ray appearances of the case reveal a typical picture of chronic fluorine intoxication affecting the skeletal tissues. An extreme degree of mottling of the teeth, nodules on the bones, marked stiffness of the spine and joints, and a diet of poor quality—all supported this diagnosis.

Discussion

The dental condition of fluorosis is very common in the province (Day), especially in certain districts of which the Ferozepur district is one. Investigations into the water content of fluorine have revealed—though the investigations so far are very limited—that in some of the districts it is very high and comparable to the figures published by Shortt and his co-workers in Madras. Though the dietary conditions in the Punjab are different from those of Madras, yet amongst the poor people in the villages the diet cannot be considered to be adequate especially in its vitamin content. (It may for example be mentioned that nutritional macrocytic anæmia is very common in the province.) In view of the existence of the above-mentioned conditions, it will not be surprising if cases of endemic fluorosis are discovered in the Punjab.

The first patient is too young for the age period of typical fluorosis, and it may be argued that the condition of bones is really a part of his anæmia, i.e. a condition allied to 'marble bones' disease. Yet the appearance of bones of this case is quite different from that condition, and there are moreover calcium deposits in his muscles and blood vessels which are not seen in that condition. We think that he developed fluorosis at an early age because, due to a chronic kidney disease, his excretory powers were deficient. The second case fits in with all the criteria of endemic fluorosis in its symptomatology, physical signs, teeth and x-ray appearances. The possibility of myositis ossificans was thought of, but was later given up because that would not show such an advanced involvement of all parts of the skeletal tissue, a spontaneous fracture and a thickened cortex of the bones which were the characteristic features of this case.

The condition remained undetected in Madras till special attention was drawn to it and the diagnosis arrived at because one of the workers happened to have some familiarity with the disease on account of his studies. It is possible that the cases described above are not isolated examples, but the disease occurs in the Punjab in an endemic form. The point can only be decided if some sort of survey is undertaken in the area from which these cases came. It is worth mentioning that both of them came from adjoining districts, and as in these districts mottling of the enamel due to fluorosis is very

common, and both these cases showed an extreme degree of mottling due to fluorosis, it is reasonable to assume that the fluorine content of water in these areas is high.

It may be argued that if the disease is really endemic in the Punjab and is due to the high content of fluorine in the water of some districts, why have only two cases been so far observed. But as seen, in Madras, such a disease can only be diagnosed if special attention is drawn towards it, and x-ray investigations of the bones are undertaken. As a matter of fact, even those two cases would have remained undiagnosed but for the published literature from Madras and but for the attention drawn towards this problem by Day in this province. After all, mottling of teeth, which is an accepted evidence of fluorine intoxication, is very common in this province, and fairly frequently mottling of an extreme degree is seen.

EXPLANATION OF THE X-RAY PRINTS

Plates XIV and XV

Case 1

Figs. 1 and 2.—The ribs and lumbar spine show marked osteosclerosis. The trabecular pattern is lost. The ribs are greatly widened and their margins are irregular. Bony excrescences are seen arising from the transverse processes.

Fig. 3.—The bones of the forearm are sclerosed. Their margins are irregular and they are widened on account of endosteal and periosteal bone deposits. The trabeculae of the bone are thickened. The radial artery and portions of the interosseous artery are calcified (the last mentioned point cannot be seen in these prints but was very well seen in the original skiagrams).

Fig. 4.—Tibia, fibula and the bones of tarsal region are sclerosed and the trabeculae are thickened. The margins are irregular on account of periosteal calcium deposits. The short deep muscles of the plantar region are calcified at their attachments to bones. The lower end of the tibial artery and its calcaneal and medial plantar branches are calcified. (The calcification of arteries is not seen in prints but can be very well seen in the original skiagrams.)

Case 2

Fig. 5.—The bones of the forearm show osteosclerosis and their margins are irregular, and at places show masses of calcification extending into the soft tissues. This is especially noticeable round the wrist bones—where there was a sinus due to the old camel bite. There is a healed fracture of the lower end of the radius—presumably due to the old camel bite. The interosseous artery is tortuous and calcified.

Fig. 6.—The margins of the tibia and fibula are irregular. The lateral surfaces of the fibulae are covered by sheaths of calcification (well seen in original skiagrams). Bony excrescences are also seen projecting into the soft tissues from the upper parts of the tibia.

Fig. 7.—The ribs show osteosclerosis, and the margins of most of them are irregular—due to calcification at the attachment of intercostal muscles. The posterior part of the right eighth rib shows a healed fracture (spontaneous).

Fig. 8.—The ligaments of the cervical spine show calcification, and long excrescences are projecting from the vertebrae into the soft tissue (well seen in the original skiagrams).

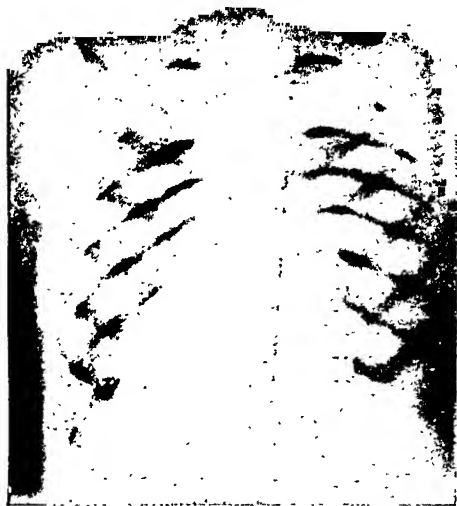


Fig. 1.



Fig. 2.



Fig. 3.



Fig. 4.



Fig. 5.



Fig. 6.



Fig. 7.



Fig. 8.

AN OUTBREAK OF TYPHUS FEVER (OXK) IN INDIA : R. N. TATTERSALL AND T. E. PARRY. PAGE 433.



Fig. 1.



Fig. 2.

Papular type of rash in typhus.

Unluckily it is impossible in these days of shortage of films to take x-ray skiagrams of all cases showing an extreme degree of mottling unless they complain of symptoms which warrant the taking of a skiagram.

Summary

Two cases are described, which we consider are definite cases of chronic endemic fluorine intoxication involving the teeth as well as the skeletal tissues.

Our sincere thanks are due to Dr. Madan Lal Aggarwal, Radiologist, Lahore, who gave us help in the reading of x-ray pictures and printing thereof.

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AN OUTBREAK OF TYPHUS FEVER (OXK) IN INDIA

By R. N. TATTERSALL
 LIEUTENANT-COLONEL, R.A.M.C.
 and
 T. E. PARRY
 CAPTAIN, R.A.M.C.

This report covers 121 cases of typhus fever (OXK) occurring in a British Regiment during October and November 1943.

The report is confined to these British cases for the following reasons:—

- (1) The incubation period was easier to determine.
- (2) The occurrence and characteristics of the rash are more easily seen on a light skin.
- (3) A more detailed and accurate history is obtainable.

The area involved is geographically adjacent to Burma, and this probably explains the close clinical relationship of the diseases to Malayan

scrub typhus and tsutsugamushi fever (Stitt, Napier). Boyd reported thirty-five cases of typhus (OXK) occurring in India, and his description of the clinical features showed a greater deviation from the Malayan type than does this series. Owing to military and geographical conditions, no survey of the literature has been possible, and the standard textbooks have been used for reference.

Epidemiology

The unit arrived from a non-endemic area on October 11. Training exercises were carried out in the region of the camp until November 2, when the unit left the area.

The accompanying figure (fig. 2) shows the day-by-day incidence of cases, the first occurring nine days after arrival and the last seventeen days after leaving the area. The maximum incidence was twelve to fifteen days after arrival.

The 'tailing off' of the epidemic may in part be due to climatic conditions, but as fresh cases continued to occur in the area throughout November and December, this cannot be considered a major factor.

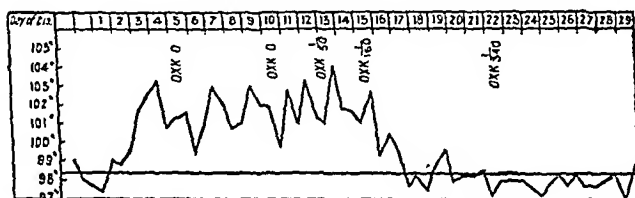
Insect vector

The only evidence available is negative in character. There was no infestation by body lice, and no patient remembered being bitten by a tick. In the eleven cases showing a definite primary lesion, this was commonly found on a covered part of the body. As it escaped notice in all cases, it seems certain that the vector is of small size.

Clinical features

Onset.—This was sudden in most cases, with shivering, sore throat and headache. In a few cases the headache preceded the fever by 2 to 3 days. One patient was admitted to hospital for a minor gun-shot wound of the thigh and developed typhus on the third day after admission. His chart (chart 1) gives an indication of the typical onset of fever.

Chart 1.



Headache.—121 cases (100 per cent).

This was a prominent symptom in all cases; usually described as frontal and retro-orbital and accompanied by a varying degree of photophobia. Both conditions persisted for the first two weeks, but usually disappeared before the fever resolved.

Sore throat.—76 cases (63 per cent).

This was usually present from the onset. The appearance varied from mild congestion

WEIL FELIX AGGLUTINATIONS TO OXK.
243 observations in 421 cases

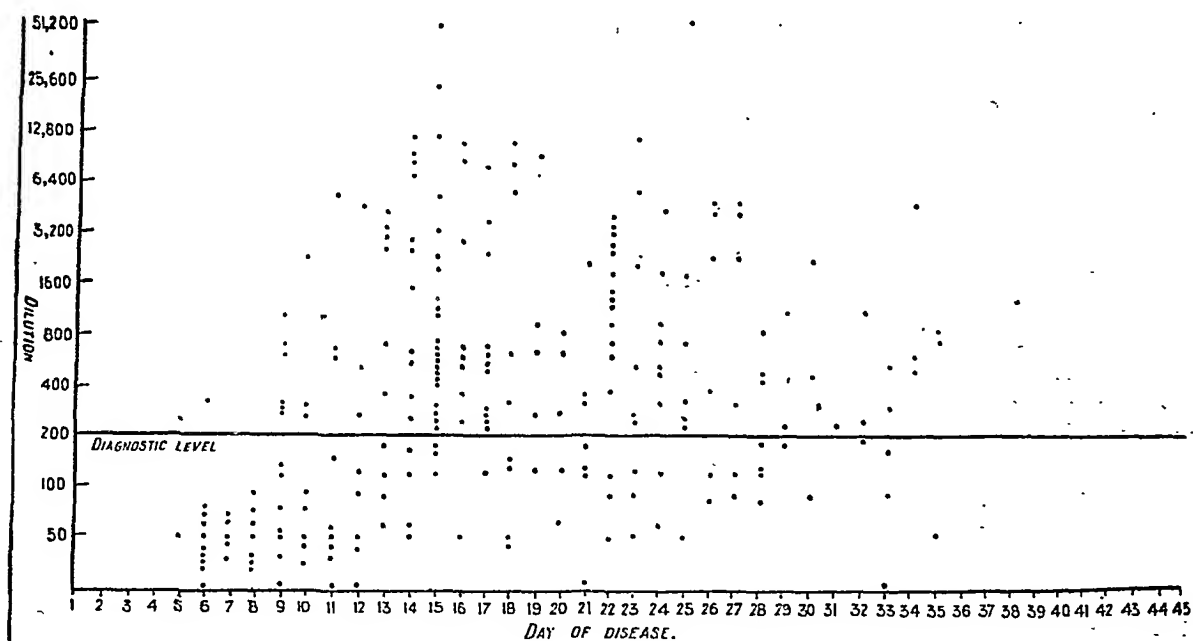


Fig. 1.

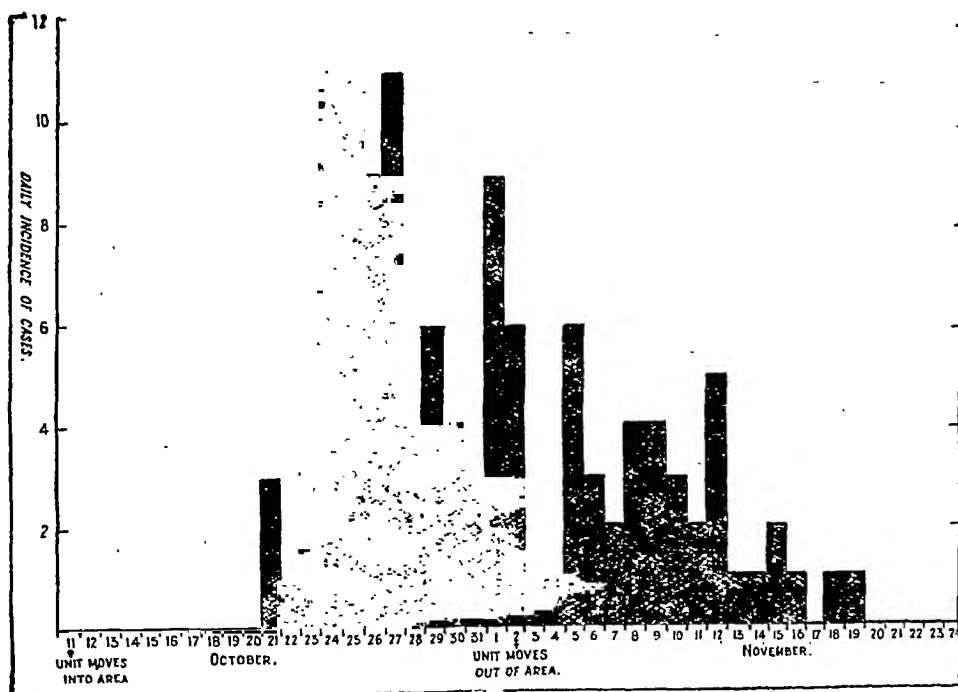


Fig. 2.

Day-by-day incidence of cases.

of the fauces to generalized œdema with gelatinous exudate. Swabs revealed no special organism on direct smear or culture. In the severe cases, there was a considerable degree of dysphagia and dysarthria. The condition normally resolved before the termination of the fever, but some laryngitis persisted into convalescence in the severe cases.

Primary lesion.—11 cases (9 per cent).

Only cases with a definite black eschar and regional glandular enlargement are included. The distribution was:—

Forearm	1
Arm	1
Leg	1
Chest and abdomen	8

Many patients had multiple bites on the legs and ankles, but in the absence of a definite

eschar these are not included. Possibly the scabs in these cases had been knocked off by the clothing.

In no case was any lymphangitis observed.

Rash.—Onset averaged the third day, the limits being the first and tenth days. Disappearance averaged the eleventh day, the limits being the fifth and sixteenth days.

The rash was macular in 39 cases and maculo-papular in 40. When scanty it was confined to the trunk and most marked over pressure points—waist and back. When profuse the limbs and face were also affected. It was equally distributed over the flexor and extensor surfaces.

The colour was brownish-red, fading on pressure, but in a few cases there was definite purpura with persistent staining. Both macules and papules were $\frac{1}{4}$ to $\frac{1}{2}$ an inch in diameter, and either circular or oval. No relationship was observed between the severity of the rash and the severity of the general symptoms.

The photographs illustrate the papular type of rash (see figures 1 and 2, plate XV).

Adenitis.—115 cases (95 per cent).

Generalized glandular enlargement was almost constantly present. The glands were discrete, rubbery, and, for the first 7 to 10 days, acutely tender on light palpation. This tenderness is regarded as an important diagnostic point. In the 11 cases with a primary lesion, the regional glands were enlarged and spontaneously painful from the onset. The average day of onset of generalized adenitis was the 3rd, disappearing on the 15th.

Mental apathy.—119 cases (99 per cent).

This symptom was very characteristic of the epidemic. When fully developed, the patient was non-responsive, silent and sleepy, with drooping eyelids and a flexed posture. In several cases this passed on to a semi-coma which lasted up to fourteen days. Subsequent amnesia covering the whole febrile period was not unusual even in those who did not develop a 'typhoid state.'

Cyanosis and flushing.—115 cases (95 per cent).

The normal flush of the febrile patient was accompanied in these cases by a brownish-cyanosed tint, usually apparent by the fourth or fifth day. This condition did not appear to be related either to the degree of pulmonary involvement or to the pulse rate. This colour usually faded before the end of the febrile stage. The mechanism of its production is considered to be peripheral rather than central. Cardiac insufficiency was not observed during the first ten days of the disease, but in the later stages and in convalescence a rapid pulse was usual. The blood pressure was lower than normal by about 20 mm., systolic and diastolic pressure being equally affected. Serial haemoglobin estimation showed no evidence of haemoconcentration.

Chest signs.—107 cases (88 per cent). These varied from a mild bronchitis to lobar consolidation, the common variety being a patchy basal-consolidation. Cough was troublesome and usually unproductive. A small number of cases had blood-stained sputum.

Conjunctival injection.—71 cases (59 per cent).

This was not accompanied by any discharge, and resolved about the 12th day without any treatment. Sub-conjunctival haemorrhages occurred in five cases.

Splenic enlargement.—42 cases (35 per cent).

In these cases the spleen became palpable between the 10th and 20th days, and was usually soft with an ill-defined edge. The maximum enlargement was during the fourth week, and in a few cases the spleen was palpable four fingers' breadth below the costal margin.

Deafness.—41 cases (33 per cent).

This was of the 'nerve' type and very variable in degree. In three cases severe deafness persisted into convalescence, though all were showing signs of recovery before discharge to convalescence.

Secondary fever.—21 cases (17 per cent).

This is defined as a late rise of fever without apparent cause such as pneumonia. The patients affected felt well during the second febrile period, and did not wish to remain in bed. Temperature charts 2, 3 and 4 demonstrate this rise.

Chart 2.

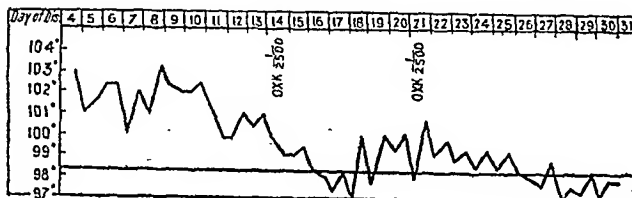


Chart 3.

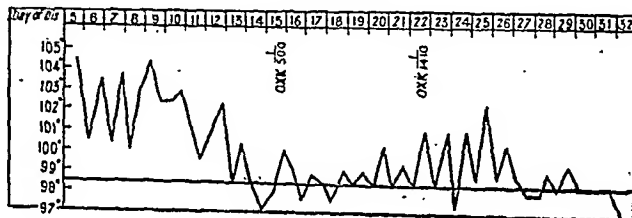
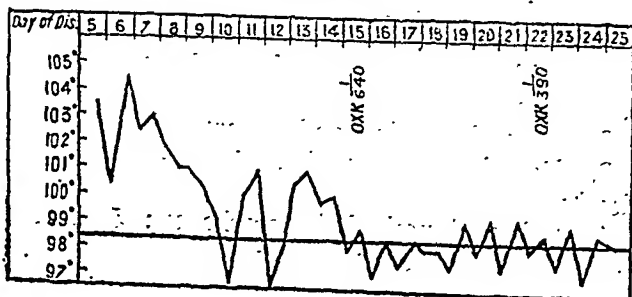


Chart 4.



Clinical diagnosis.—By the fourth day of fever it was found possible to make the diagnosis on clinical grounds. Even in the absence of a rash, the apathetic, flushed and cyanosed patient with a tender adenitis was so characteristic of this disease that confusion was impossible.

Pathological diagnosis.—The Weil-Felix agglutination of OXK was usually diagnostic by the 13th day. The maximum readings were obtained between the 13th and 22nd days, and after this the titre tended to fall. The result of 240 agglutinations of OXK are graphed in figure 1 and demonstrate this rise and fall in titre. Agglutination of OX19 and OX2 strains occurred in dilutions of $\frac{1}{16}$ to $\frac{1}{64}$, in most of the cases with a high titre for OXK. Agglutination of OXK in $\frac{1}{200}$ dilution was regarded as diagnostic. The high titre Weil-Felix test was performed in two cases. The Dreyer's reduction tables were used in the interpretation of the results.

Leucocyte counts.—An average of the counts by weeks is shown below. Counts for the first and sixth weeks are too few to be of statistical value :—

Week	Total	Polymorphs.	Lymphocytes	Monocytes	Eosinophils
2nd	5,400	47	46	6	..
3rd	7,100	49	42	6	..
4th	6,800	54	40	4	(Eosinophilia in 25 per cent.)
5th	8,210	45	40	5	8 per cent (eosinophilia in 50 per cent).

Less than 5 per cent eosinophils was not considered as eosinophilia. The maximum eosinophilia in any one case in the fourth week was 25 per cent, and in the fifth week 42 per cent.

Deaths.—Age was of no significance in prognosis, the average being 28 years for both fatal cases and survivors. Deaths occurred on the 12th, 12th, 13th, 15th, 16th, 17th, 19th, 24th, 25th and 26th days of illness. Increasing cyanosis with a rising pulse rate preceded death by 12 to 36 hours.

Convalescence.—Joint and muscle pains in the legs and shoulders were usual during the first week out of bed. A raised pulse rate and diminished exercise tolerance persisted for 3 to 4 weeks.

Complications.—Few and not particularly serious.

1. Oedema of the ankles: 2 cases—only temporary.
2. Pleural effusion and hæmoptysis: 1 case.
3. Retrobulbar neuritis: 1 case—recovering slowly.
4. Sub-conjunctival hæmorrhages: 5 cases—all with complete recovery.

5. Relapsing vivax malaria: many cases.
6. Three cases of neuritis involving muscles of the shoulder girdle.

Treatment

1. Sulphapyridine—useful when lobar consolidation or polymorphonuclear leucocytosis was found; of no value in the treatment of the rickettsial broncho-pneumonia commonly occurring in these cases.
2. Mepacrine—given as (0.1 gramme thrice daily), during the febrile period as an anti-malarial suppressive measure; proved very useful.
3. Calcium lactate—ten grammes thrice daily; no beneficial results noticed.
4. Convalescent serum—10 c.cm. given intramuscularly; no improvement noticed.
5. Fluids—given in large quantities. No difficulty was experienced in administration as the patients with sore throats complained of thirst. This was sometimes so intense as to cause insomnia.
6. Lumbar puncture—gave temporary relief when the headache was severe. The C.S.F. pressure was slightly raised; there was no increase in cells.

Diet.—A 2,500 calorie diet with 'marmite' and ascorbic acid was given in the febrile phase. Anorexia was marked, and even this amount was difficult to administer. During convalescence a 5,000 calorie, high protein, 'malnutrition' diet was given, as most cases showed some degree of emaciation.

Summary of clinical findings

1. Total cases 121
2. Incubation period 9 to 17 days
3. Average fever 18 days
4. Deaths 11 cases

Sign or symptom	Number of cases	Percentage
Primary sore	11	9
Splenomegaly	42	35
Sore throat	76	63
Deafness	40	33
Apathy	119	99
Conjunctivitis	115	95
Chest signs	107	88
Rash	79	66
Adenitis	115	95
Secondary fever	21	17

Post-mortem findings (11 cases)

External appearance.—No constant abnormality detected. All were young men of normal physique.

Cardio-vascular system.—Dilatation of the right side of the heart with a flabby myocardium was found in ten cases. No abnormality of valve cusps or arteries.

Respiratory system.—An extreme degree of pulmonary congestion was found in ten cases. Broncho-pneumonia was present in four cases, and lobar pneumonia in two. Ulceration of the epiglottis, hæmorrhages into the trachea and pleural effusion were each present in one case.

Spleen.—Normal in two cases. In the remainder it was large, soft and friable. This appearance was very characteristic of the disease.

Liver.—No constant alteration in size. The nutmeg appearance of chronic venous congestion was found in six cases.

Kidneys.—Congestion marked in all cases.

Suprarenals.—Normal in all cases.

Gastro-intestinal.—Small fleshy glands were numerous in the mesentery in all cases. Petechial hæmorrhages were present in the stomach, ileum, cæcum or colon in five cases.

Brain and meninges.—Some congestion in all cases.

Post-mortem investigations

Brain smears were examined for rickettsial bodies and malaria parasites with negative results in all cases.

Weil-Felix agglutinations were done with the heart's blood in six cases. The results to OXK were 85, 160, 300, 340, 500 and 560. Numbers 1 and 2 had given titres of 250 and 300 during life. The other five cases gave diagnostic OXK agglutination titres during life. Owing to absence of facilities, no histological work was possible.

Experimental animal transmission

On the advice of Dr. S. R. Savor, white mice were used for this purpose. 1 c.cm. of ground clot from a patient in the second week of the disease was injected intraperitoneally into a mouse. This mouse died on the 12th day, and rickettsial bodies were demonstrated in the scanty peritoneal fluid obtained.

Brain and spleen emulsion from this mouse was injected intraperitoneally into a second mouse. This died on the 8th day, and rickettsiæ were numerous in the very scanty peritoneal fluid. In the third passage the mouse was killed on the 12th day. Abundant sterile peritoneal fluid present but no rickettsia found. In the fourth passage the mice showed no evidence of the disease.

Summary

The clinical and epidemiological aspects of an outbreak of typhus fever OXK are discussed.

The rise and fall of the Weil-Felix titres (OXK) are graphed, showing maximal readings between the 13th and 22nd days.

The development of eosinophilia during the fourth and fifth weeks is noted.

The characteristic post-mortem findings of dilatation of the right heart, pulmonary injection and enlarged mesenteric glands are described.

A simple method of animal transmission and demonstration of rickettsia is described.

Our thanks are due to Dr. Savor for his advice on the technique of animal transmission and to Lieut.-Colonel M. H. P. Sayers, R.A.M.C., for his help and advice during the epidemic.

ONE HUNDRED AND FOURTEEN CASES OF TYPHUS FEVER SEEN IN AN INDIAN MILITARY HOSPITAL IN CALCUTTA

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IN 1912 Bradley and Smith (1912) described a case of fever with a rash in a British soldier in a camp near Barrackpore fifteen miles from Calcutta. They suspected typhus, and their description is very suggestive of the disease.

In 1922-23 Basu (1924) described fifteen cases of fever with a rash occurring in Calcutta, and which he considered to be typhus.

No further cases have been reported from the Calcutta area. Since the war however many cases have been seen both in British and Indian troops. As Dr. Napier pointed out (Editorial, 1936; Napier, 1943) the 'detecting power' of troops for disease, when they are introduced into India, is considerable. They need not be British troops. Indian troops when moved outside their own areas are prone to pick up disease to which they have not been exposed in their own country.

The cases described here were all in Indian troops. Clinically they were all similar. Serologically they could be divided into two types. One agglutinated proteus OXK. It is accordingly often referred to as 'K' typhus. It closely resembled the condition described by Lewthwaite and Savor (1940) as the Malayan typhus which has been called scrub, rural, or tropical typhus. In Malaya a mite has been proved to be the vector and the disease is sometimes called mite typhus. The other serological type agglutinated proteus OX19. They were perhaps on the whole milder than the OXK cases. In most parts of the world a mild typhus is found in towns, associated with rats, and with shops in which rats are often found. It has been called murine, urban, or shop typhus and, where the rat flea has been proved to be the vector, 'flea' typhus.

The cases were seen in the hospital between the middle of June and the end of December 1943.

Sixty cases were forwarded by a field hospital from a village about eighty miles from Calcutta on the Jessore Road. Fifty-four cases came from Calcutta itself.

Below is a table of the fortnightly incidence of the two main serological groups, with the clinical cases and one OX2 case, a peculiar variation :—

varieties appear indiscriminately in rural and urban areas.

The difference in mortality rates I am unable to explain. The country group were almost entirely in fighting troops. The Calcutta cases were mainly in ancillary troops.

Vector

Enquiries have given no indication of a possible vector. The officer commanding the field hospital was unable to obtain any history

COUNTRY CASES

Month	June	July		August		September		October		November		December	
Fortnightly periods ..	16-30	1-15	16-31	1-15	16-31	1-15	16-30	1-15	16-31	1-15	16-30	1-15	16-31
OXK	2	5	7	8	12	7	8	12	6
OX19	1	..	1	1
Clinical	1	1

CALCUTTA CASES

Month	June	July		August		September		October		November		December	
Fortnightly periods ..	16-30	1-15	16-31	1-15	16-31	1-15	16-30	1-15	16-31	1-15	16-30	1-15	16-31
OXK	1	3	1	6	5	4	1	4	4	4	4	4
OX19	1	1	4	2	1
Clinical	1	1	..	1
OX2	1

It will be noted that in the cases from the country, 55 out of 60 were serologically OXK. Six cases (10 per cent) were fatal. Of the six fatal cases, four were OXK and two were diagnosed on clinical and post-mortem findings. Three out of sixty were serologically OX19.

It is not possible to say what the troop movements were in the area, but troops were there prior to July. The incidence would seem to be fairly steady throughout the rains and well into the dry weather.

It will be noted that in the Calcutta area, forty-two out of fifty-four cases were serologically OXK, eight agglutinated OX19 and one agglutinated OX2, while three were diagnosed on clinical and post-mortem findings. The mortality in the fifty-four Calcutta cases was eleven (20.3 per cent). Seven of the eleven were serologically OXK. One was OX2. Three were diagnosed on clinical and post-mortem findings.

The mortality in 114 cases was seventeen (14.9 per cent). Anigstein (1933) records a mortality of 13.6 per cent in Malaya. The Calcutta group had the larger number of OX19 cases, but I do not think any conclusions can be drawn from this. It has been noted by Maitra and Sen Gupta (1936) in Burma that in 109 cases of typhus the 'scrub' and 'shop'

of bites, nor did repeated questioning of my patients produce any results. No lice or nits were ever found on the patients. In about six of the first cases, the clothing was very carefully examined for lice with negative results. Thereafter the clothing was examined in many but not in every case, again with negative results. No local lesion or local adenitis suggestive of a microscopic bite was ever found. This is the case in most reports on typhus in India. The only observations made were, that of the two regiments mainly concerned in the country outbreak, the incidence was much higher in the regiment doing most jungle training. The figures were thirty-six as against eleven. A unit which arrived in Calcutta and which began to clear some bamboo jungle near their camp had four cases shortly after their arrival.

Clinical description of the disease

The onset is usually sudden and is often associated with a rigor, though coincident malaria may have occasionally been responsible for this. Rigors were sometimes noted however in cases in which the blood was repeatedly negative for parasites.

Headache, apart from the headache present with fever in general, is often troublesome.

Occasionally there was a complaint of generalized body pain. Six cases complained of deep-seated chest pain not very definitely localized. Four cases complained of vague abdominal pain for which there was no obvious explanation. It is usually difficult to elicit information from the patient during the disease; hence one gets the impression that headaches and pain are only complained of if severe.

The tongue is usually coated, and constipation, as a rule, is present.

Congestion of the conjunctivæ was present in nineteen cases (16.3 per cent).

The pulse is not rapid; it is slower than one would expect in relation to the temperature, and thus resembles that of typhoid. The pulse rate, of course, increases with increasing toxæmia, or if the patient becomes delirious. The spleen is often felt, but coincident malaria may be often responsible. In fatal cases in which the spleen was not palpable, some degree of enlargement of the organ was frequently noted at autopsy. Signs of bronchitis were elicited in 72 cases (62 per cent). Cough is not often troublesome; if present, it is unproductive.

The lung signs may be heard during the first few days but may be delayed for seven to ten days. Scattered rhonchi may be heard all over the chest, or a few medium-pitched non-resonant crepitations (crackling râles) over the lungs posteriorly, or both rhonchi and crepitations (râles) may be heard.

During the course of the disease, congestion of the lungs may increase, and the percussion note may become impaired. There was never any alteration in the vocal fremitus or resonance.

Sometimes pneumonia was suspected and sulphapyridine or sulphathiazole given, but no apparent improvement in the patient's condition or in the physical signs was ever seen, nor was any pneumonic consolidation seen in fifteen autopsies. In one case there was microscopically early broncho-pneumonia. I therefore feel that pneumonia is not a common complication in cases seen here.

By the end of the first week the patient has become quite drowsy. It is difficult to get him to reply to questions, and then it is often only 'yes' or 'no' to leading questions.

The pathological process may then concentrate on the lungs or the brain, or in the milder cases improvement may set in. The chest cases develop more signs of congestion in the lungs, and they suffer from air hunger. The sputum coughed up is scanty, white and frothy.

The cerebral cases become more stuporous. They either lie like logs, or are irritable and restless. Neck rigidity was noted in a few cases but was always slight.

By the end of the second week and middle of the third week most patients have begun to recover. Gradually the chest condition begins to improve. They become less drowsy, and the temperature begins to subside. They can be

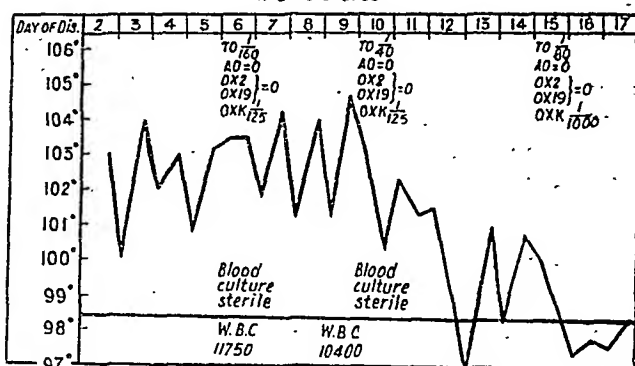
more easily coaxed to take fluids and food, and improvement continues.

The form of the temperature chart is variable. In general one may say that it is a continuous fever, with perhaps occasional remissions, which falls by lysis. Relapses are occasionally seen; these do not, as a rule, cause any trouble to the patient.

In cases with coincident malaria there is nothing in the form of the chart to suggest that malaria is present. While malignant tertian fever may be maintained at a high level for 36 hours, the usual intermittent fever is not seen even in coincident benign tertian relapse infections.

The fatal cases, however, towards the end of the second week show no signs of improvement. Incontinence often develops. Subsultus tendinum and facial twitching are noted. Coma develops and deepens, and the outlook is undoubtedly grave. Yet I have seen many patients look desperately ill and still recover.

Chart I.
A severe case



An important negative finding was the absence of any enlargement of the superficial lymph glands in practically every case. There were only two exceptions to this. One case had lymph glands enlarged in the left groin and left axilla. The other case was one noted at autopsy with enlargement of the cervical glands.

Another important negative finding was that in most cases no rash was ever seen. In only fifteen cases (13.1 per cent) was it noted.

The most striking rash, immediately apparent on inspection, was in the only case which agglutinated OX2. Dull red macules averaging the size of an anna piece were distributed over the trunk and limbs. It was present on admission on the tenth day and was fading but visible at death on the twenty-second day.

The other fourteen cases agglutinated OXK. In them the rash was not easily seen. Had it not been that all cases suspected of having typhus fever were being closely inspected, some of them might easily have been missed. The rash seen consisted of faint reddish-brown macules, difficult to see against a pigmented skin, in size about two to five millimetres in diameter. It was usually noticed first over the

upper abdomen and spread centrifugally over the trunk and sometimes arms and thighs; as far as I could judge it appeared towards the end of the first week but usually began to fade after three or four days leaving no pigmentation.

Fatal and severely ill cases more commonly had rashes than less severe cases. In addition to the macular element, a dull red erythema was occasionally present.

The following additional signs were noted :—

Bleeding from the gums was a troublesome feature in the fatal OX2 case. A transfusion of whole blood was given and the bleeding stopped.

Hæmaturia was noted in two cases. One of these was fatal, and at autopsy hæmorrhagic spots were found in the wall and mucous membrane of the bladder.

Hæmoptysis.—Three patients coughed up blood-stained sputum. Naturally tuberculosis was thought of. In one the sputum later became 'rusty', but no pneumonia developed as far as could be judged. No acid-fast bacilli were found. The second patient complained of hæmoptysis with fever. An x-ray report was that the lungs showed evidence of tuberculous infiltration. At post mortem a week later, no evidence of tubercle was found.

The third patient, 'a follower', was sent in with a history of fever for three months and hæmoptysis for two days. He was afebrile.

that for a time he was having rigors on alternate days for which he was treated as an out-patient with a sweet-tasting medicine (certainly not quinine). His Wilson-Weil-Felix was ~~200~~ ultimately falling. It seems reasonable to suppose that he had malaria and a concomitant attack of typhus prior to admission.

Mental confusion was noted in two severely ill patients. It persisted into convalescence but cleared up completely.

Abdominal colic was an occasional complaint.

Severe earache was complained of in one case for no obvious reason.

Deafness was complained of in one case well into convalescence.

The temperature charts of four typical cases belonging to different groups are appended.

Complications

The only complication seen in my cases was parotitis which was noted in two cases. Sulphapyridine had no effect as far as I could see. It was painful but otherwise there were no ill effects.

The duration of the fever.—This varied, and perhaps partly, because the onset of typhus was not easy to fix with certainty when malaria is also present. The following tables show the figures obtained from the patient's statement as to when his illness began in the ninety-nine cases which recovered. In fifty-five of these (57.9 per cent), the duration of the fever was between twelve and twenty days.

Duration of the fever in the 54 non-fatal country cases, grouped in three-day periods

Duration of the fever in days	6-8	9-11	12-14	15-17	18-20	21-23	24-26	27-29	30-32	33-35	Unknown
Number of OXK cases ..	1	4	12	10	11	5	3	2	..	2	1
Number of OX19 cases ..	1	1	..	1

Three examinations of the sputum were negative for acid-fast bacilli, and an x-ray showed no abnormality in the lungs. It was elicited

The duration of the fever in thirty-four out of fifty-four (63 per cent) non-fatal cases was between twelve and twenty days.

Duration of the fever in six fatal cases from the country

Duration of the fever in days	6-8	9-11	12-14	15-17	18-20	21-23	Unknown
Number of OXK cases ..	1	2	1
Number of cases of clinical typhus.	..	1	1	..

Duration of the fever, grouped in three-day periods, in the forty-three non-fatal Calcutta cases

Duration of the fever in days	4	6-8	9-11	12-14	15-17	18-20	21-23	24-26	27-29	30-32	33-35	Unknown
OXK cases	1	0	2	5	7	7	2	4	1	..	2	1
OX19 cases	3	4	2

The duration of the fever was between 12 and 20 days in twenty-one (51 per cent) of the 41 non-fatal Calcutta cases.

Duration of the fever in days in the eleven fatal Calcutta cases

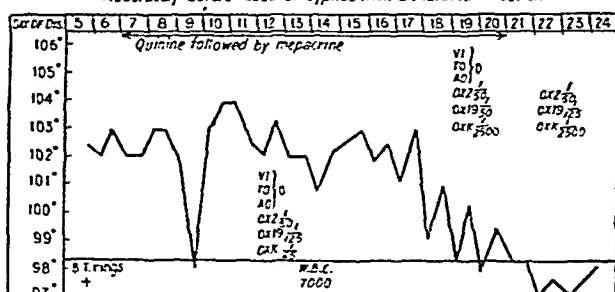
Day of disease on which death occurred	9-11	12-14	15-17	18-20	21-23	24-26
OXK cases	4	..	1	2
OX2 case	1	..
Clinical cases	1	2

On clinical and post-mortem evidence four died within 14 days when serological evidence is often not positive.

The mild cases

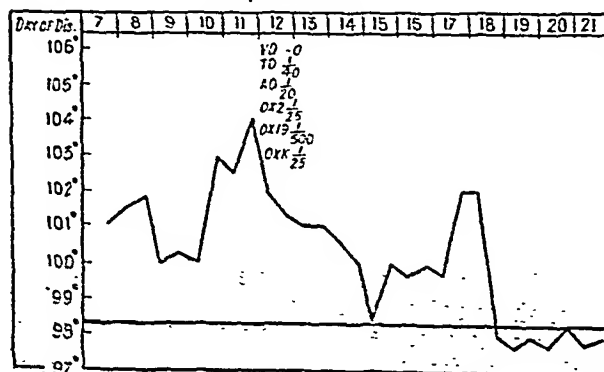
One has been impressed by the mildness of a number of cases of this disease. Many, while running a temperature, were walking about the wards in the evening, and eating a full diet. Others have fever, a slight cough, and signs of bronchitis. They clear up in little over a week,

Chart 2.
Moderately severe case of typhus with a malarial infection



and only a positive Wilson-Weil-Felix test enables one to make a diagnosis of typhus.

Chart 3.
A very mild case.



Laboratory and clinical side-room examinations

The total white cell count was carried out in eighty-four cases. It was within normal limits

of 4,000-11,000 (Whitby and Britton, 1944) in 64 (73.8 per cent).

Studies of the total white cell count and of the rise and fall in different types of cases were made. These studies revealed no definite correlation between the count and the severity of the disease and gave little indication of any prognostic value in the rise or fall in the count.

The total white cell count within normal limits has this value, that it is not suggestive of typhoid fever on the one hand, or of a pyogenic infection on the other.

The differential count was not often carried out, owing to pressure of work. Fifteen cases examined however gave the impression that there is no significant change. Whitby and Britton (1944) say that a lymphocytosis occurs in typhus. Presumably their findings are in the European or classical louse-borne variety. There was no suggestion of a lymphocytosis in the few cases examined here.

No information therefore is likely to be gained from occasional blood examinations, except in excluding other diseases in which definite blood changes are expected to occur.

Blood cultures were carried out in sixty-eight cases. Fifty-two were sterile and sixteen contaminated.

Stool and urine culture was negative for pathogens in twenty-six cases examined.

Blood pressure.—This was estimated in nine cases, and the figures were always low and were of the order of 95/70. There did not seem to be any difference between a very mild and a more severe case. In two fatal cases it was 95/35 and 90/50.

Cerebro-spinal fluid.—Greenfield and Carmichael (1925) mention changes found in the cerebro-spinal fluid in European typhus. These are said to be: pressure always raised except in moribund cases, cells moderately increased (i.e. 10-50 per cent), protein slightly or moderately increased (40-180 mg. per cent), chloride slightly reduced or increased, urea constantly increased and the Wilson-Weil-Felix either frequently positive according to one observer or always positive early in the disease (according to other authorities).

In twenty of my cases the C.S.F. was examined, though not always for the various substances mentioned above. The pressure was 160 or over in fifteen cases out of twenty tested. Normal figures are 60-120 mm. (in the recumbent posture) according to Wright (1940) and 60-150 according to Greenfield and Carmichael (1925). The highest figures were 360 mm.

Protein was raised in two out of eleven cases estimated. These two were a fatal case and a severely ill case.

Chloride was slightly reduced in four cases examined; urea was within normal limits in four cases.

In five cases the cells were 5, 5, 9, 3, 3 per c.mm., the latter two being fatal cases.

The number of estimations, chemical and serological, is small. My feeling however is that apart from a raised pressure noted in some cases, no constant or wide variation from normal is found.

I consider that if a manometer is available the measurement of the pressure of the cerebro-spinal fluid should be carried out in patients who are being lumbar punctured for any reason.

If the pressure is raised and the symptoms are suggestive of typhus, the raised pressure supports the diagnosis. Otherwise no information from the cerebro-spinal fluid is likely to be of value. However, more information is required.

Serum calcium.—van Meerendonk (1942) reports low figures for serum calcium in European typhus. His figures are of the order of 6.0 mg. per cent. Normal figures range from 9 mg. to 11.5 mg. per cent as given by Stitt *et al.* (1938) or according to Wright (1940) fairly constantly 10 mg. per cent.

The serum calcium level in the blood depends on several factors, amongst others the plasma protein level (Evans, 1939); unfortunately no serum protein estimations were carried out. The figures I obtained in fourteen cases suggested a slight fall in serum calcium in some cases, but there was no correlation between the

appearance, are in some way related to injury of the capillaries and arterioles of the brain. The lesions are also seen in other organs.

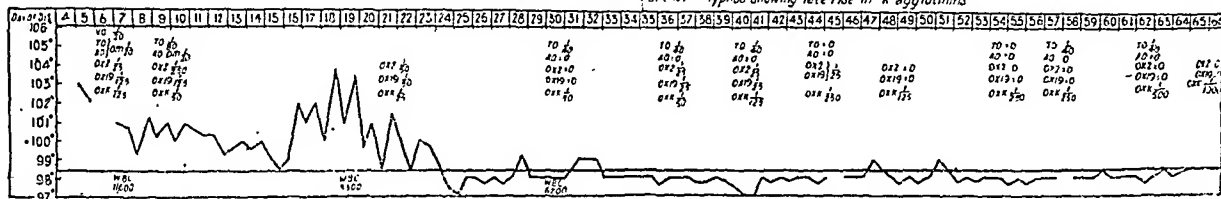
The subsequent hæmorrhage may be seen in the lungs, pleura, pericardium, bowel mucosa and bowel wall, bladder mucosa and bladder wall, kidney tissue and pia-arachnoid membranes. Similar naked-eye appearances may be seen in any septicæmia.

Sub-pleural hæmorrhages were seen in seven cases, sub-pericardial hæmorrhages in one. Patchy congestion of the lungs was seen in seven cases, and generalized uniform congestion in four. Recent pleural adhesions were seen in five cases and old adhesions in one case. A hæmorrhagic pleural effusion was seen in one case. The lower half of the trachea and the bronchi were congested in four cases.

Intramural hæmorrhages in the bowel wall were seen in three cases.

The mucous membrane of the small bowel showed patchy congestion in two cases. The mucous membrane of the cæcum showed the same sort of patchy congestion in three cases, and the mucous membrane of the colon patchy congestion in one case. Small hæmorrhagic areas were seen in the stomach in three cases, in the small bowel in six, the ileo-cæcal valve in three, the cæcum in two and the colon in one

Chart 4. Typhus showing late rise in *K agglutinins*



Differential diagnosis.—Typhus must be considered in all cases of continuous fever in this area.

Typhoid and paratyphoid fevers.—These fevers have typically a more gradual onset. The patients do not usually appear stuporous during the early stages. A positive blood culture is of course an absolute differentiation. The total white cell count is low in typhoid and generally within normal limits in typhus.

Improvement in the third week in a patient who has been very ill suggests that the fever is not typhoid or paratyphoid fever. The rash is not very often helpful, but a profuse rash is uncommon in typhoid; often only repeated agglutination tests will enable a diagnosis to be made. A rise in titre of T_0 in those inoculated with T.A.B. vaccine may be misleading. But even with a T_0 titre of $\frac{1}{16}$ the test should be repeated and unless sustained may be disregarded.

Conversely a titre of $\frac{1}{128}$ OXK may be found in typhoid cases.

Meningitis.—Irritability, headache and drowsiness may suggest meningitis.

In typhus there may be slight stiffness of the neck. Kernig's sign may be positive but it is not marked.

A lumbar puncture must be done. In typhus the fluid may be under pressure but it is clear, and the cell count is within normal limits. If there is doubt, a sulpha drug should be given. Culture of the fluid should be carried out in the meantime. A Weil-Felix test is unlikely to be positive but further information is required on this point. A total white cell count within normal limits would be consistent with typhus, a raised white cell count suggestive of meningitis. These counts should be repeated.

Small-pox.—This disease in its early stages may be difficult to differentiate. If small-pox is epidemic it will be thought of, and if the vesicles develop the diagnosis is made. The morbilliform prodromal rash of small-pox closely resembles typhus, but a typhus rash rarely appears in the first 48 hours, as does the prodromal small-pox rash.

When the true small-pox eruption appears, it appears centrifugally. Also in a very short time it becomes papular and shotty.

A blood film examined in the early stages of severe small-pox sometimes shows immature white cells.

Such a slide from a fatal case of small-pox was examined by Major Parker, R.A.M.C., officer-in-charge, District Laboratory, Calcutta. He told me that it closely resembled blood slides he had seen in British soldiers with typhus in an Assam outbreak. These slides were taken early in the disease.

Glandular fever.—As there was associated glandular enlargement the possibility of this disease was considered. In the Indian cases seen here glandular enlargement was rarely seen. In glandular fever the abnormal cells

are present after the onset. The results of the Weil-Felix and a Paul-Bunnell test should enable doubtful cases to be differentiated.

Measles has some points of similarity, the congested eyes, the mental dullness and the sudden onset. The differentiation is more difficult in cases with an extensive rash—as seen in the Mysore cases described by Heilig and Naidu (1941, 1942).

The demonstration of Koplik's spots in the mouth suggests measles. Typhus does occur in children but it is not often reported. Measles is unusual in adults.

Tuberculous meningitis is not likely to be confused if the complete history is available, with a slow onset, and developing signs of intracranial pressure. The cerebro-spinal fluid will of course give information, pleocytosis with diminution of the chlorides being suggestive of tubercle and possibly tubercle bacilli being found to settle the diagnosis.

Paratyphoid C.—I have seen a case which clinically resembled typhus—with marked conjunctival congestion. Paratyphoid C was cultured from the gall-bladder at autopsy.

Dengue.—This common disease requires differentiation. Though the form of the temperature curve may be suggestive—that of dengue remaining high for a few days, falling slowly, and then showing a terminal rise at the end of seven days, there may be a more continuous type. The main differences are the absence of drowsiness and lung signs in dengue, and the presence of pains in the eyeballs with photophobia in dengue. If the fever continues during the second week, typhus will be considered—and the Wilson-Weil-Felix may decide the diagnosis. Mild typhus and dengue may be differentiated only by the agglutination tests. There is a neutropenia in dengue, not a very helpful point in differentiation.

Pneumonia.—The physical signs of a frank pneumonia are absent in uncomplicated typhus. The respirations may be increased in rate but are not suggestive of pneumonia, there being no respiratory grunt. The absence of a leucocytosis will be suggestive of no pneumonic process being present. If there is doubt about the presence of pneumonia either as a primary disease or complicating typhus, an appropriate sulpha drug should be administered. An apical pneumonia which frequently gives rise to marked cerebral symptoms must always be looked for.

Malaria.—This disease is of course always considered in the diagnosis of any tropical fever. If parasites are found, the response to treatment will decide in a few days whether malaria is responsible for the fever.

Treatment.—McRobert's article (1925) reads well to-day. I did not see it until I had treated quite a number of cases, and I can endorse all he says. The supply of adequate fluid in this as in any other fever is, I am sure, of considerable value. Restlessness did seem

to be controlled by the intravenous saline drip—three to six pints in twenty-four hours.

This will not of itself control cerebral irritation however. Morphia should not be withheld if required. I have recently noted the effect of intramuscular paraldehyde in doses of 6 to 8 c.cm. The results seemed entirely satisfactory. I cannot however find any reference to this method of giving what is admittedly an admirable hypnotic. Sulphapyridine and sulphathiazole had no effect on the disease, but if pneumonia is suspected, one of this series should be exhibited, preferably not sulphapyridine, owing to the risk of kidney complications in febrile subjects.

Atebrin has been claimed by van Meeren-donk (1942) to have a specific action. Megaw, in remarks on the article, was not convinced. Patients having coincident malaria treatment (including atebrin) did not seem to have any advantage over those who were not being given atebrin.

The Wilson-Weil-Felix reaction.—Wilson (1909) of Belfast was the first to describe this peculiar reaction. Its value in the diagnosis of typhus is accepted.

It is well to remember that there may be a raised titre of the Wilson-Weil-Felix in two diseases—undulant fever, and leptospirosis, according to van Rooyen (Kemp *et al.*, 1933; Foshay, 1940; Calder, 1941). These are of the order of $\frac{1}{16}$ for undulant fever and $\frac{1}{8}$ for leptospirosis. I am suspicious of an $\frac{1}{16}$ OXK titre in kala-azar, and would like to have continued readings in some proved kala-azar cases. Anigstein (1933) considered that a rising titre with alcoholized suspension (*i.e.* O forms) to $\frac{1}{16}$ OXK was diagnostic in clinically suggestive cases.

In my cases, $\frac{1}{16}$ was considered diagnostic in suggestive cases. Some cases were accepted in which the highest titre was $\frac{1}{16}$ where clinically the diagnosis did not seem in doubt and where the titre had risen. Anigstein also considers that severe cases often have a low titre. This is not invariably so.

One also must remember that illiterate patients may present themselves with fever and a history of fever for some months. Their Wilson-Weil-Felix may be suggestive or even strongly positive. Yet their fever may be other than typhus and their agglutinins may be residual from typhus fever of many weeks previously.

My cases were serologically ninety-six OXK, twelve OX19, and one OX2. Five cases were diagnosed on clinical and post-mortem findings. The Wilson-Weil-Felix usually becomes significant in endemic murine typhus at the end of the first or at the beginning of the second week. The diagnostic rise in titre in scrub or K typhus is often delayed until the end of the second week or until convalescence.

Major Parker was able to isolate a 'K' strain of rickettsia from one of my cases in the District Laboratory, Calcutta.

I would stress a few important points about the Wilson-Weil-Felix test.

One test is in itself rarely of value. It is important to carry out serial examinations.

The diagnostic titre is sometimes present for only a few days.

It is sometimes present late in convalescence.

It is never too early to begin, and never too late to give up hope in suspected typhus.

In some cases there is an associated rise in OX2 and/or OX19. In a few cases OX19 rises and then falls and OXK later rises to high titre.

There seemed to be no association between the agglutination figures and the severity of the disease.

One has been impressed by the number of mild cases. The sort of case that one thinks of is a man who has had fever for a few days. He has signs of bronchitis. His temperature is continuous for a few days and falls by lysis. He is weaker than one would expect, but is otherwise well, and it is only a positive Wilson-Weil-Felix that enables a correct diagnosis to be made. Some cases are labelled malaria, and have malaria, since parasites are found in their blood but their response to specific therapy is slow. Some cases in the same way are considered to be bronchitis.

Summary and conclusions

(1) 114 cases of 'tropical' typhus seen in Calcutta in 1943 are described, with notes on 16 autopsies.

(2) A little over half came from a village 80 miles from Calcutta, the rest were admitted from all over greater Calcutta.

(3) The mortality was 14.9 per cent, of which 11 were serologically OXK, five were diagnosed clinically, and one was OX2.

(4) A rash was present in 13.1 per cent of the cases; usually it was not prominent.

(5) Many of the cases were not severe.

(6) No vector was identified.

(7) Calcutta is an area where infective vectors are present during the second six months of the year, at any rate judging by one year's experience.

Jungle may be uniformly saturated with infective vectors or these may only occur in patches. The rains and early part of the dry weather would seem to be the likely period of the year to contract typhus.

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INFECTIVE HEPATITIS

ANALYSIS OF 100 CASES IN THE ARMY

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This disease is also known as 'epidemic catarrhal jaundice', 'acute infective hepatitis' and 'epidemic infective hepatitis.'

During this war, great interest has been shown in this disease by the medical profession owing to various problems presented which had to be solved quickly. It broke out in epidemic form among the Middle East forces, affecting not only the Allies but the enemy as well; and along with malaria and venereal disease it has become one of the most important diseases in that theatre of war. Its high incidence, the long stay in hospital, and the absence of any method of prevention make it a serious problem.

In Ceylon, jaundice, usually called catarrhal jaundice, has existed in sporadic form and has been considered a mild disease. Its incidence among individuals, groups, or bigger communities was not high. The accepted pathology

of a transient catarrhal condition of the bile passages and duodenum did not worry anybody seriously.

Among Ceylonese service men, our statistics show that it was not until 1943 that the disease appeared to any appreciable extent. Most of the cases in this series have been from Colombo, Jaffna and Trincomalee, three important towns in Ceylon. It would be interesting to know the incidence and distribution of this disease among the civil population during 1943 and 1944. As a serious view is now taken of this condition, the health authorities should consider the possibility of outbreaks among school children, labour gangs and colonists settled in newly reclaimed areas. In the case of children, especially, it should be remembered that among Egyptian school children some cases of cirrhosis of the liver are found not due to bilharzia, and are suspected to be due to infective hepatitis which is endemic around the Mediterranean coast (Witts, 1944). Though not a fatal disease, its relatively long course and convalescence, and the liver damage involved, are factors worthy of consideration from the preventive and economic aspects.

Recently two other conditions very similar to infective hepatitis have been described, *viz*, homologous serum jaundice and post-arsenical jaundice. In this series are included 12 cases of post-arsenical jaundice.

Epidemiology

In the Middle East, infective hepatitis has been most common in autumn and early winter. Admissions to this hospital show that peaks occurred during the hot months in this country, *viz*, March-April and July-August, with moderate rises in October-November, the lowest being in December-January.

Little difference has been reported in the outbreaks among school children and troops (Witts, 1944). The straggling nature of the outbreaks and the benign course of the disease in Ceylon have already been mentioned. Outbreaks among Ceylonese troops have not been of a serious nature, cases of jaundice forming only 1.12 per cent of all admissions during 1943 and 1944. It is by no means a highly infectious disease, as during these two years there have been only two cases of cross infection in this hospital.

In outbreaks among the Middle East forces, Europeans have shown a greater susceptibility to the disease than Asiatics and Africans. British officers were found to be more susceptible than other ranks. But among the Americans, the incidence has been equal among officers and men. This greater British officer incidence has been attributed to the greater outside contact of officers, their common use of crockery and cutlery and also to the more unhygienic condition of their kitchens and mess rooms (Witts, 1944).

Though the living condition of the British officers and Ceylonese officers are the same, the officer incidence among Ceylonese troops has been low, only 6 per cent of cases treated in this hospital. This fact and the absence of records of outbreaks of epidemic infective hepatitis among civilians in Ceylon either in children or adults may be due to resistance of the Ceylonese in general.

The administration of arsenic, gold and alcohol are also said to increase the susceptibility to the disease (Damodaran and Hartfall, 1944). One of the patients in this series, a medical officer, had four days' fever which did not prevent him from doing his normal work. Then he was afebrile for three days. On the last day, he took too many drinks at a party; on the next day he was admitted to hospital with fever and subsequently developed jaundice. Undue stress and strain affecting troops in the field, insanitary surroundings, lack of personal hygiene and extremes of temperature are some of the predisposing causes. Overcrowding is a potent factor in the spread of the disease as cases of our series indicate.

Ætiology

Many experimental investigations carried out by various workers have resulted in no definite conclusion about the causative factor. The theory that it is due to filter passing virus has been generally accepted. The following facts are adduced in support of this view: long incubation period, occurrence of epidemics, general constitutional symptoms and rarity of second attacks.

So far all animal experiments have proved negative, *e.g.* intramuscular injections of affected human serum into horses, but intramuscular injection of blood serum from a patient has caused infective hepatitis in a healthy subject (Cameron, 1943). Nasal instillation of nasal washings from a patient has also been successful in inducing the disease (Findlay *et al.*, 1944). The interval between the injection and the appearance of symptoms is said to be shorter in the latter case. The period of infectivity is said to be very short, and if these experiments are to be successful, material should preferably be taken in the earlier stages of the disease. These facts and the localization of the infection suggest that the mode of transmission is by droplets.

Very close contact is necessary for infection (Edwards, 1943) and the possibility of transmission through contact with excreta has also been suggested owing to the frequency with which nurses became infected (Evans, 1942). None of the nursing staff in this ward, however, has yet contracted the disease, in a period of over two years.

There is an instance of a medical man in our series who was in daily contact with a large number of cases of jaundice. His two children got the infection within 12 weeks of each other.

This raises the question of the possibility of a carrier-borne infection in this disease without affecting the carrier himself.

Owing to the almost universality of gastrointestinal symptoms, and also to the control of certain outbreaks by attention to water supply, contaminated water supply has been suspected as a source of infection. But most records of epidemics do not lend support to this mode of infection and do not show the explosive nature associated with it (Pickles, 1939). Occasionally it is said that the virus may find its way into the water supply giving rise to explosive outbreaks of infection. In a certain outbreak, infection was traced to a polluted water supply; but the suspicion could not be proved conclusively (Cookson, 1944). In this outbreak there have not been at any time any large number of cases occurring in one unit using a common water supply.

Fly, mosquito, bed bug and various other insects have been suspected as carriers, but there are no sufficient grounds for any conclusion on this point.

Pigs and horses have been suspected to be hosts or reservoirs for the infecting agent. The endemicity of the disease in strictly Muslim countries rules out the possibility of pigs as hosts; there is a type of jaundice which horses suffer from and is due to piroplasmiasis, the vector being ticks.

Incubation period

This has been reckoned by most workers to be about 30 days. Two cases in this series developed jaundice whilst in hospital. They were admitted for other ailments and were in for long periods. Each had a case of hepatitis in the next bed. In these two cases it was possible to reckon the incubation period which was approximately 4 weeks. A medical officer in this series came in contact with two cases of jaundice and contracted the disease exactly a month later. Among three cases of infective hepatitis admitted within a short period from one camp consisting of 30 to 40 men, the first gave no history of contact but the last two cases contracted the disease 30 and 35 days after the first one.

On the other hand, in the two children of the medical man referred to previously, infective hepatitis occurred within 12 weeks of each other exhibiting identical clinical features. These children might have acquired the disease from their father or, as they attended different schools from different sources. In another instance, two medical orderlies quartered in the same hut contracted jaundice within 110 days of each other; here again the possibility of infection from two different sources complicates the problem.

The incubation periods of homologous serum jaundice and post-arsenical jaundice are very much longer, as will be seen from the table.

Latent periods of 12 cases of post-arsenical jaundice reckoned from date of first injection of neoarsphenamine to appearance of symptoms of hepatitis

Case number	Disease for which injections were given	Latent period in days	REMARKS
1	Venereal	241	Spleen +.
2	Asthma	172	Pulmonary acariasis.
3	Venereal	135	Spleen +.
4	Asthma	125	Pulmonary acariasis.
5	Venereal	101	Relapse mild.
6	Do.	117	
7	Asthma	107	Pulmonary acariasis.
8	Venereal	45	No history of contact with a case of jaundice.
9	Do.	111	Ryle's tube used to drain duodenum.
10	Do.	180	Relapse mild.
11	Do.	123	
12	Do.	141	Spleen +.

Pathology

Virchow was the first to describe the pathology of catarrhal jaundice as a duodenitis and cholangitis with plugging of the ampulla of Vater. Van den Bergh made it possible to differentiate causes for the appearance of jaundice. The scarcity of post-mortem material has, in former years, prevented workers coming to a correct understanding of the pathology.

There are still those who think that catarrhal jaundice with its traditional pathology exists *per se*. A post-mortem report on a patient suffering from catarrhal jaundice, who met with an accidental death, describes a catarrhal condition of duodenum, stomach, and bile duct but no damage to liver or pancreas. A separate condition of acute infective hepatitis is also described with no pre-icteric symptoms (Price, 1941). In our series and the series published by others, there have invariably been a pre-icteric stage as fever, anorexia and epigastric pain which are also present prior to onset of catarrhal jaundice.

There has not been a single death in our series and so no post mortem was possible. Where post-mortem material was available, and by biopsies, the following findings are recorded. Sub-acute necrosis of the liver; the liver not greatly altered in size, and cut section showed a granular appearance on a yellow background; intra-lobular bile ducts normal; degeneration of liver cells at the centre of lobules; hæmorrhages into serous cavities such as the pleuræ and also into kidneys and stomach and subcutaneous tissue (Cameron, 1943).

Liver function tests done by various workers showed a deficiency in the majority of cases.

Mode of onset

The onset is usually insidious. The patients in this series have had various premonitory symptoms such as headache, general malaise, sore throat, and coryza, and one case was admitted for acute tonsillitis. Nausea and vomiting are fairly common; loss of appetite is almost a universal complaint but one case in this series never had anorexia and the appetite was quite good. Fever of a mild type was found in 71 per cent of cases. In one case (an officer) there was continuous high fever for seven days before jaundice appeared. In a place like Ceylon, an attack of malaria may coincide with an attack of hepatitis, and in such cases temperatures are usually high. In this series no intermediate stage and no second rise of temperature before the onset of jaundice, as mentioned by Cameron (1943), occurred. These premonitory symptoms last for about 3 to 10 days and rarely longer, before the onset of jaundice. Exceptionally, these premonitory symptoms may be absent, and a high-coloured urine and jaundice attract the attention of the patient for the first time. One case was admitted with low fever; blood showed no parasites; on the second day, the patient became restless and showed symptoms of mental disturbance. On the fourth day, conjunctival icterus appeared and the mental symptoms and fever subsided.

Clinical features

A summary of the predominant clinical features in this series are given in the following table:—

Analysis of predominant clinical features in 100 cases of infective hepatitis

Symptoms and signs	Frequency, per cent	REMARKS
Bilinuria—bile pigments	98.00	Main complaints were anorexia, upper abdominal discomfort, nausea, vomiting, epigastric pain. Always mild except when complicated with malaria.
Gastric	78.00	
Fever	71.00	
Clay-coloured stools ..	48.00	Varying from 1 to 6 per cent.
Liver palpable ..	39.00	
Previous history of malaria.	36.00	
Bilinuria—bile salts ..	35.00	
Monocytes ..	28.00	Others mostly constipated. Mostly not severe.
Tenderness over right hypochondrium only.	16.00	
Diarrhoea	15.00	
Itching	14.00	

TABLE—concl'd.

Symptoms and signs	Frequency, per cent	REMARKS
Leucocytosis ..	13.00	10,000 to 16,000.
Spleen ..	12.00	Eight gave p.h. of malaria.
Malarial parasites in ..	7.00	Mostly B.T.
Previous history of jaundice. .	5.00	
Albuminuria ..	4.00	No casts of any kind found.
Bronchitis ..	2.00	One had bile-stained expectoration.
Relapses ..	2.00	Both post-arsenical jaundice.
Van den Bergh done in 51 per cent of cases :—		
Biphasic ..	39.21	
Delayed direct ..	41.11	
Immediate direct ..	13.12	
Negative ..	6.56	

Fever is usually of a mild type, which generally subsides with the onset of jaundice, but may rarely continue even during jaundice.

Gastro-intestinal symptoms.—Anorexia is a common complaint. Then comes upper abdominal discomfort and nausea. Vomiting and epigastric pain are fairly common; the former may be severe and persistent as found in a few cases in this series. Two cases complained of severe pain in the right iliac fossa simulating appendicitis so closely that the surgeon's opinion was called for. Constipation is the rule, but diarrhoea is fairly common. In this series, 15 per cent had diarrhoea and one of them had blood and mucus in stools.

The liver.—Usually the degree of enlargement was about two fingers' breadth below the right costal margin. 39 per cent of cases had liver enlargement with tenderness, and another 16 per cent of cases had only tenderness over the right hypochondrium without enlargement of the liver. This enlargement disappeared in about 10 to 14 days. The gall-bladder was not palpable in a single case.

The spleen was enlarged in 12 per cent of cases; only 4 of these did not give a history of malaria. In these four the splenic enlargement was apparently due to infective hepatitis. Cameron (1943) found 46 cases of splenic enlargement out of 176 patients, i.e. 27 per cent. According to this, in a place like Ceylon, where malaria is endemic, our series should have had a greater percentage of enlarged spleens.

The respiratory tract.—Few patients had a mild inflammation of the upper respiratory tract such as sore throat and coryza. Two cases developed bronchitis during the course of the disease. In one case, bronchitis was severe and persisted for a long time and the expectoration was markedly bile stained.

The cardio-vascular system.—Moderate bradycardia (pulse 55 to 65 per minute) was noted

in a large number of cases. Most cases showed a leucopenia with a tendency to relative lymphocytosis. Monocytes ranging from 1 to 5 per cent were found in 25 per cent of cases. Thirteen per cent showed a leucocytosis.

Van den Bergh reaction.—This was done in 51 per cent of cases with the following results: 20 cases (39.21 per cent) gave a biphasic reaction; 21 cases (41.11 per cent) gave a delayed direct reaction; 6 cases (13.12 per cent) gave an immediate direct reaction; and 4 cases (6.56 per cent) gave negative results.

Blood sedimentation rate.—Only very few blood sedimentation rates were done but no abnormality was found. Hawley *et al.* (1944) found a raised rate in about 60 per cent of cases.

Genito-urinary system.—Bile pigment was found in 98 per cent and bile salts in 35 per cent of cases. The latter was found almost always with the former. In some cases pigments disappeared in one day, to reappear in the next day. Disappearance of bile in the urine for three consecutive days was the prelude to return to normal health. Albumin was found in 4 per cent of cases but deposits showed no casts of any kind. Dysuria occurred in only one case.

The urine was clear of bile in :

1-7 days in 39% of cases
8-14 " " 43% " "
15-21 " " 9% " "
Over 21 " " 9% " "

Two cases had bile in the urine for 51 and 42 days respectively.

Skin.—No rash of any kind was found in this series. Fourteen per cent complained of itching. It was so very severe in one case that alkaline baths and sleeping draughts had to be resorted to.

Eyes.—Blurred vision and photophobia were seen in 2 per cent of cases.

Central nervous system.—Only one case showed mild mental symptoms as already referred to. Insomnia was rare.

Malaria.—31 per cent gave a history of malaria. Seven per cent had actual fever and malarial parasites were found in their blood.

A few patients complained of vague pains in the joints and muscles especially those of the back.

Previous attacks.—These were recorded in the histories of 5 per cent of the series.

Diagnosis

Anorexia, upper abdominal discomfort and low temperature in a person who is otherwise well should make one suspect infective hepatitis even before the onset of icterus. Urine will be of a very high colour and the froth will be of a greenish tint. In epidemic infective hepatitis, cases without manifest jaundice are now well recognized (Findlay *et al.*, 1944).

The writer saw one such case and the course of the icterus was very mild and short.

The histamine test has been considered a valuable help in the diagnosis of latent jaundice (Cameron, 1943), but Gordon (1943) states that this test was disappointing.

Differential diagnosis

(1) *Weil's disease*.—This is due to *Leptospira icterohæmorrhagica* which can be isolated from the urine. There is leucocytosis, very high fever with extreme prostration. History of occupations which have to do with rat-infested areas as sewers and dockyards is important.*

(2) *Malaria*.—The 'bilious remittent' type of malaria usually due to falciparum infection also causes jaundice. In jaundice due to malaria, a reticulocyte response is noted (Findlay *et al.*, 1944). Apart from this, both diseases might co-exist. The presence of malaria parasites will confirm the diagnosis of malaria, and in general there is no enlargement of the liver or tenderness in the right hypochondrium, which are usually present in infective hepatitis. Blood sedimentation rate is raised in malaria about 10 mm. per hour while in infective hepatitis it is below that in the first 10 days (Wood, 1945).

(3) *Influenza*.—It might be difficult to differentiate the two till icterus appears. Waring (1943) thinks that infective hepatitis is a variety of influenza.

(4) *Yellow fever*.—This disease should not be forgotten in endemic areas.

Other diseases which might have to be differentiated, are typhoid fever, appendicitis and diseases causing jaundice, such as carcinoma of the head of pancreas.

Prognosis

There were no deaths at all in this series. Generally the death rate is said to be low, but prolonged stay in hospital and a long period of convalescence are necessary. Only two cases had relapses, one after a month and the other after two months. Both were very mild cases and were in hospital for only one week.

Owing to the possible liver damage, the remote prognosis is not altogether rosy. A long convalescence and the avoidance of alcohol and other hepatotoxins are advisable.

Treatment

Twenty-six per cent of cases were treated with glucose, insulin and ascorbic acid as advocated by MacDonald (1943), 15 per cent were treated with glucose and ascorbic acid only and the rest were treated in the usual way with glucose and calcium lactate. A concentrated solution of mag. sulph and sodii sulph equal parts, 2 drs. was given to every patient in the morning as a routine.

With these different forms of treatment there was no appreciable difference in the disappearance of bile from the urine, and thus the average duration of stay in hospital was almost the same.

In very persistent cases with prolonged icterus and enlargement of liver, repeated intravenous injections of calcium gluconate 10 c.cm. gave very satisfactory results. Large doses of hexamine with sodium bicarbonate 1 dr. of each, twice a day for 24 to 48 hours, are well worth a trial in resistant cases specially where itching is very severe.

In two persistent cases, Ryle's tube was used to drain the duodenum. The disappearance of bile from urine for 3 consecutive days was taken as the criterion of a cure irrespective of the conjunctival icterus which lasts very much longer.

Discussion

That infective hepatitis, post-arsenical jaundice, and homologous serum jaundice, are due to an infection and that by a virus is accepted by all workers. The incubation period of post-arsenical jaundice as from the date of the first injection to the appearance of the initial symptoms of jaundice ranged from 45 to 241 days in the 12 cases in this series. This is a big variation and rather raises a doubt whether the virus of infective hepatitis is the same as that producing post-arsenical jaundice. Findlay *et al.* (1944) believe that the agents responsible, and the hepatitis following yellow fever inoculation and arsenic belong to the same group and are antigenically related, and state that the variation in incubation period is not inconsistent with virus causation. It may perhaps be also explained adequately by the individual resistance in our series.

On the other hand, Hawley *et al.* (1944) observed that the hepatotoxic agent causing post-arsenical jaundice and homologous serum jaundice is not the virus of infective hepatitis. Complement fixation tests done by various workers differ in their results, *e.g.* MacCallum and Bauer (1944); Findlay *et al.* (1944).

In post-arsenical jaundice, although the hepatic lesions among others are not like those produced by arsenical poisoning (Dibble and MacMichael, 1943), it is not easy to exclude the toxic factor of arsenic altogether and as Forbes (1944) states, this problem awaits final solution.

The mode of transmission by droplet infection is accepted almost universally. But in the case of post-arsenical jaundice and homologous serum jaundice, it has been suggested that transmission may be by inoculating infective material during injections [Beattie and Marshall (1944)] or the presence of virus in the blood, plasma or serum [Findlay *et al.* (1944)]. There is also the possibility of contact infection. Whether a patient suffering from post-arsenical jaundice can infect another is another problem. One case of post-arsenical

*Not in India; where most houses are rat-infested, occupation is of little importance.—Editor.

jaundice in our series visited his brother just before his illness and was with him for three days only. The latter developed jaundice just 32 days after his brother.

Splenic enlargement in this series is very low compared to the statistics published by others. Ordinarily, one would expect a large percentage of splenic enlargement in a place where malaria is endemic. In cases with splenic enlargement, one should ascertain whether they suffered from attacks of malaria before.

Skin rashes and joint and muscular pains were not common. One interesting feature was bile-stained expectoration of one of the patients who contracted bronchitis. Bradycardia was never prominent, the pulse rate ranging from 55 to 65 and only for a short time. A rapid pulse is not uncommon in the pre-icteric stage.

Blood sedimentation rate readings have given different results with different workers. Before accepting the observations of Wood (1945) on the blood sedimentation rate to differentiate between infective hepatitis and malaria, further work is necessary.

A van den Bergh test was done in 51 per cent of cases and the results were variable, giving all three types of the direct reaction. This variation seems compatible with the pathological changes found in the liver.

Various methods were employed in treatment, but no particular method was found to be of any special advantages. Still, in persistent cases, intravenous calcium gluconate and large doses of hexamine with alkali were found to be beneficial. There were two cases of relapse and both were mild attacks.

In some cases when malaria and infective hepatitis co-existed, the routine anti-malarial treatment was given. The writer had no reason to withhold mepacrine, and is of the opinion that it makes no difference to the course of the hepatic condition.

Only 5 per cent of cases in this series gave a history of similar attacks of jaundice previously, showing possibly that the disease confers a high degree of immunity, but not an absolute one.

Prevention

This is a very important aspect of this problem owing to the long stay in hospital, long convalescent period and the serious damage to the liver.

Overcrowding, unhygienic surroundings, indulgence in alcoholic beverages should be avoided. Contacts should be isolated for two weeks as advocated by Pickles (1939). This procedure becomes very necessary in outbreaks occurring in camps and schools. It has been found unnecessary to close schools, but the teachers should be instructed in the early detection and isolation of contacts. During convalescence, hepatotoxins of all kinds should be excluded. Beattie and

Marshall (1944) state that it is desirable to give 2.5 to 3.0 gm. methicnine or one pint of milk daily to prevent post-arsenical jaundice. As the hepatic changes in both these diseases are similar, it would be advisable to adopt similar measures when the threat of an outbreak is imminent. The condition being accepted as a virus disease; the possibility of prophylactic immunization should be considered.

Conclusions

1. Personal resistance seems to be an important factor.
2. The incubation period in epidemic infective hepatitis ranges from 28 to 35 days, but may be much longer. The latent period in post-arsenical jaundice is very variable. The pre-icteric stage may be from 3 to 10 days, in rare instances up to 14 days.
3. Splenic enlargement has not been a prominent clinical feature in this series.
4. No particular method of treatment has any special advantage in shortening the course of the disease, but intravenous calcium gluconate and large doses of hexamine and alkali are valuable in resistant cases. In cases of infective hepatitis and malaria, routine malaria treatment (including mepacrine) does no harm.
5. Immunity from second attacks seems to be very high, but not absolute.

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HEPATIC ABSCESS SECONDARILY INFECTED : PENICILLIN TREATMENT

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THE list of organisms sensitive to penicillin is growing, and it is likely that some organisms originally classed as non-susceptible may be brought within its sphere of influence, with variations in the technique of administration. The following case is of interest in that two of the organisms concerned have been regarded as almost completely insensitive, and yet in this instance seem to have been affected by penicillin.

Case report

Lieut. H. A. C., a British officer, aged 35, was admitted on the 20th November, 1944: he complained of pain in the right side of the chest and feverishness.

One month previously he had been admitted to another hospital where he was first treated with sulphapyridine (26 grammes in 6 days) for pneumonia and diaphragmatic pleurisy, and was later diagnosed as amoebic hepatitis. A course of emetine hydrochloride was begun on the 29th October, 1944; one day later he experienced a sudden onset of sharp pain in the right lower chest; the liver was found to be enlarged downwards to the level of the umbilicus; x-ray showed an egg-shaped elevation of the central portion of the right diaphragm and the heart displaced to the left; irregular, intermittent fever had persisted throughout this period; his W.B.C. count was 17,200, of which 86 per cent were polymorphonuclear cells, 8 per cent lymphocytes, 4 per cent monocytes, and 2 per cent eosinophils. Fluid aspirated from the right pleural cavity was sterile on culture. Aspiration was again done on the following day, i.e. the 31st October, 1944; this time from the upper portion of the right lobe of the liver; it produced a thin, red fluid, in which were suspended grey flakes, and in these *Entamoeba histolytica* were found; cultures from this fluid were sterile.

After ten injections of 1 grain emetine hydrochloride, this drug was discontinued on the 7th November, 1944. By the 10th November, 1944, his 'liver' dullness had decreased to the fourth anterior intercostal space above, and to three finger breadths below the right costal margin. His irregular temperature had settled, and his leucocytes numbered 7,400. On the 17th November, 1944, fever having recurred, he presented dullness up to the level of the right second rib, and x-ray demonstrated a right pleural effusion. Next day, 240 c.c.m. of hæmorrhagic fluid was aspirated from the chest; aspiration again, on the day following this, produced 150 c.c.m. of blood-tinged pus.

On transfer to this hospital on the 20th November, 1944, 'liver' dullness extended from the level of the fourth right rib to one inch below the level of the umbilicus; the W.B.C. count was 13,200. Emetine hydrochloride injections were recommenced on the 22nd November, 1944. His general condition improved and he remained afebrile. On the 4th December, 1944, 20 c.c.m. of chocolate-coloured pus was aspirated from the right chest: it contained pus cells, but was sterile on culture. On the 5th December, 1944, emetine hydrochloride was discontinued; he had had 12 injections in this second course. His liver had decreased

in size to three finger breadths below the costal margin, and upper dullness was limited at the seventh rib in the mid-axillary line.

On the 7th December, 1944, he had a rigor, followed by irregular high fever with frequent peaks above 103°F. Repeated blood smears were negative for malarial parasites. By the 11th December, 1944, he had severe right shoulder pain; his W.B.C. count was 16,400, of which there were 76 per cent polymorphonuclears, 20 per cent lymphocytes, 3 per cent monocytes, and 1 per cent eosinophils. Emetine bismuth iodide, in 3-grain doses per day, was begun on the 12th December, 1944; but no appreciable effect resulted. On the 15th December, 1944, x-ray showed a large cavity, with a fluid level in line with the fourth right rib. Since the 11th December, 1944, he had been gravely ill and at times appeared moribund.

On the 18th December, 1944, two pints of pus was aspirated; and 200,000 units of penicillin in 90 c.c.m. of normal saline was injected into the cavity. The pus was thick, grey coloured, very foul and faecal smelling. Microscopic examination of direct smears showed numerous cocci and bacilli, both gram-negative and gram-positive; on culture, *Bacillus coli*, *Staphylococcus albus*, and *Bacillus faecalis alkaligenes*, were isolated: no anaerobes were found. The penicillin was given more in the spirit of a 'last hope' than as a specific remedy; indeed, it is not unlikely that, had the infecting organisms been identified at the time instead of 48 hours later, penicillin would not have been used. A course of sulphathiazole, 6 grammes per day, was also begun on the 18th December, 1944. On the 20th December, 1944, a white cell count was 20,000; his general condition showed considerable improvement.

On the 25th December, 1944, the administration of sulphathiazole, of which 40 grammes had been given, was stopped. Fever, with peaks about the 100°F. line, persisted. X-ray, on the 26th December, 1944, demonstrated a fluid level in line with the fifth rib. On the following day, 2½ pints of thick, yellow pus was aspirated, and a further 200,000 units of penicillin in 150 c.c.m. normal saline was instilled. This pus differed from that withdrawn on the 18th December, 1944: the colour had changed from grey to light yellow, the foul odour had completely disappeared, and cultures, both aerobic and anaerobic, were sterile. On the 28th December, 1944, rib resection (mid, posterior, tenth right rib) was done: a unilocular, thick-walled abscess cavity extending upwards to above the level of the fourth rib and downwards to the level of the umbilicus, and of an estimated capacity exceeding 5 pints, was found; about 3 pints of non-odorous, light yellow pus was released; a de Pezzer catheter was inserted, and closed, water-seal drainage instituted.

The pus, found at operation, was again sterile on cultures. Purulent drainage continued freely for 48 hours, and then it altered to a deep yellow, translucent fluid. This fluid was repeatedly cultured and was sterile; it continued to drain in decreasing quantity. By the 6th January, 1945, the capacity of the abscess was 6 ounces; the operation wound had healed primarily around the de Pezzer tube; he had been apyrexial since operation; and the lower liver margin reached to one finger breadth below the right costal margin. Three weeks later, the abscess cavity was less than 2 ounces capacity, and in a further fortnight, drainage had ceased and the wound along the tube passage had almost completely healed.

Discussion

Florey (1944) includes *Bacillus coli* in the list of organisms almost or completely insensitive to penicillin. *Bacillus faecalis alkaligenes* is a member of the dysentery group which is regarded as insusceptible (M. R. C., 1944).

It is possible that in this case penicillin acted upon the staphylococcus and that sulphathiazole

was responsible for the elimination of the *B. coli* and *B. faecalis*: but, in view of the dramatic change in the character of the pus, which, at the time of the first instillation of penicillin, was grey and foul-smelling and gave positive cultures, as contrasted with that found at the next aspiration when the pus was yellow, odourless and sterile, and particularly for an abscess of such gross dimensions, it would seem that sulphathiazole alone could not have dealt so effectively with the gram-negative enteric organisms. There remains a strong impression that either penicillin was the chief sterilizing agent, or that the combined effect of the two drugs was a mutually reinforcing one and amounted to more than the sum of their separate actions.

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ACUTE POLYARTERITIS NODOSA IN A CASE OF MALARIA

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CASES of polyarteritis nodosa are sufficiently rare to justify a report. This is all the more so as we are not in a position to define the ætiological factor that is responsible. The clinical diagnosis is difficult and many cases are discovered only at autopsy. Recently it has been recognized that the condition is more common than was thought, and not universally fatal; healed polyarteritis is occasionally diagnosed. Involvement of the kidney may lead to hæmaturia followed by a picture of essential hypertension; involvement of the mesenteric or coeliac vessels may give rise to acute abdominal symptoms suggesting cholecystitis or other conditions, while involvement of the arteries of peripheral nerves results in a polyneuritis; a syndrome of progressive cardiac failure from ischæmia due to scarring of the myocardium is well recognized; cerebral and meningeal types have also been reported. The complexity of the symptoms and their tendency to change from organ to organ as in this case is of some importance in diagnosis.

Case report

The patient D. W. E., aged 27, a lance-corporal, was admitted to a British Military Hospital on 7th December, 1943, for fever with rigor and vomiting coming on every day for the past 3 days. There was a definite history of malaria a year ago, but examination of the blood on admission did not show parasites. The patient complained of slight pain in the right flank in the region of the kidney. The urine on microscopical examination showed a few red blood cells.

leucocytes and epithelial casts, but culture was negative. A short course of sulphanilamide therapy (12 tablets) was carried out without much effect. The pain and tenderness in the right flank increased. A week after admission, ring forms and trophozoites of *Plasmodium vivax* were found in the blood and treatment was started with quinine. However, the pain in the abdomen was not relieved, but spread to the chest. There was also tenderness in the renal area on the right side. Some stiffness in the muscles of the neck was noticed and also a positive Kernig's sign. A lumbar puncture on 15th December, 1943, showed spinal fluid under normal tension and with a normal cell count. The fluid culture was negative. The blood at this time showed a moderate leucocytosis (16,200 W.B.C.) with a differential count of polymorphonuclear cells 75 per cent, lymphocytes 19 per cent, eosinophils 2 per cent and monocytes 9 per cent. The pain in the abdomen persisted, and a slight upward enlargement of the liver was suspected. There was slight distension of the abdomen. During this period the temperature was varying from about 99° in the mornings to 101° in the evenings. The pulse rate varied from 100 to 120, the respiration from 20 to 24, while the blood pressure showed a reading of 118/86. The Wassermann reaction was positive +-. The blood culture and the Widal reactions were negative. On 24th December, 1943, there was severe hæmoptysis at night; the abdominal pain increased in intensity, but there was no rigidity. Pain in the chest was also persistent. Slight attacks of hæmoptysis continued for about 10 days; for this the patient was treated with injections of horse serum. A fine maculo-papular rash had developed on the arms and face. The sputum showed no acid-fast bacilli on repeated examination. The pain across the chest and abdomen increased, the hæmoptysis persisted and the patient died suddenly on 2nd January, 1944, on the 25th day of admission.

Autopsy findings.—At autopsy (2nd January, 1944), the body was somewhat emaciated and anæmic, and the abdomen was distended. There was extensive hæmorrhage into the peritoneal cavity which contained about 26 ounces of fluid blood. This was from a rupture of an aneurysm of the hepatic artery just below the gall bladder. The aneurysm was of the size of a hen's egg with a tear about 6 mm. long on the under surface. The heart (215 gm.) was slightly atrophied. Under the epicardium there were multiple pea-like nodules along the course of the superficial branches of the coronary arteries (figure 3, plate XVI). On section, some of the nodules were found to be small aneurysms filled with dark red blood clots, while other smaller nodules were made up of greyish-white tissue involving the vessel wall. The descending branch of the left coronary artery was specially involved. The valves and valvular openings were normal. There was neither infarction nor scarring of the myocardium. The muscle was brownish-red and the ventricles were reduced in size. The right lung (270 gm.) showed a small aneurysm of the bronchial artery of the size of a pea (figure 6, plate XVI). This was in relation to the main bronchus at the hilum. The lung tissue appeared normal. The left lung (240 gm.) showed no aneurysms or visible thickening of the vessels. The liver (1,140 gm.) was atrophied, brownish-red in colour, with a smooth capsule, and distinct lobular markings on section. Multiple aneurysms varying in size from a pea to a lemon were scattered in the substance of the liver in relation to the branches of the hepatic artery in the portal systems (figures 4 and 7, plate XVI). The gall bladder was compressed and its cavity reduced in size by the pressure of the aneurysm below. The spleen (105 gm.) was atrophied and on section showed aneurysms in the region of the hilum. The right kidney (150 gm.) showed on the surface a number of pale irregular depressions due to scarring; aneurysms of variable size were scattered in the boundary zone; one in the cortex of the size of a marble was on the point of rupture. The left kidney (140 gm.) was similar in appearance except that the aneurysms were confined to the boundary zone (figures 1 and 5,

plate XVI). The pancreas also showed multiple aneurysms, varying in size from a pea to a bean. The branches of the mesenteric artery showed chains of small nodules at their junction with the small intestine (figure 2, plate XVI). The nodules on section were small fusiform swellings which had not developed into aneurysms. Similar fusiform nodules were found on the branches of the celiac axis as well as the mesocolic vessels. The aorta showed only moderate atheroma and no other abnormality. The brain (1,200 gm.) was normal. No aneurysms were found on the circle of Willis and its branches, nor in the small vessels in the substance of the brain.

The following therefore were the main findings: (1) emaciation; (2) anaemia; (3) 26 ounces of free fluid blood in the peritoneal cavity; (4) aneurysm of the hepatic artery which had burst and caused hæmorrhage; (5) multiple small aneurysms along the course of the vessels of the liver, spleen, kidneys, pancreas, and heart; (6) small periarterial nodules in the coronary arteries, the mesenteric arteries and in the branches of the celiac axis. Death was due to polyarteritis nodosa and rupture of a large aneurysm of the hepatic artery with hæmorrhage into the peritoneal cavity.

Histological findings.—The typical necrotizing arteritis that is the essential feature of the disease was found in the small arterioles of the bronchioles, the kidneys, the liver and the pancreas, while gross aneurysms were found in almost all the organs examined except the brain, the thyroid, the pituitary, the adrenals and the testes. The vessels of the skin and the muscles were not grossly involved. The necrotizing lesion specially affected the internal elastic lamina and the muscle fibres of the media in the small arterioles. It was a fibrinoid necrosis, the fibrinoid material staining intensely with eosin and being different in nature from hyalinization. The inner part of the media, the elastica and the sub-intimal tissues were all involved, while in very small vessels the endothelium was split and shed in layers, and in places proliferated. The involved muscle fibres and elastica of the vessels showed some degree of cedema.

The smaller vessels distal to the lesion showed a characteristic change. This was a splitting of the internal elastica into several layers as demonstrated by the Verhoeff elastic stain. Nearer the zones of fibrinoid necrosis, the small vessels showed patchy fragmentation and swelling of the split elastic layers.

Another characteristic change was an acute periarteritis involving in many vessels the adventitia, but in some the media and intima were specially involved. The inflammatory reaction was subacute in type, showing polymorphonuclear cells, plasma cells, mononuclear cells, lymphocytes and occasional eosinophil cells with a variable proliferation of the fibroblasts. The areas of periarteritis and endarteritis were generally distinct, but occasionally all the coats were involved. A frankly

suppurative reaction was not seen. Micro-organisms could not be demonstrated in the inflammatory tissue.

The whole appearance suggested that the early lesion was due to some agent in the blood which had successively involved the intima, the elastica and the media, while the periarteritis was more a reaction to the changes inside. Where the necrotizing arteritis involved the larger arterioles and arteries, the lesion was mostly patchy and gave rise to local gaps in the muscle and elastic layers. Where these had not yielded, local proliferation in the intima had formed a protective layer encroaching into the lumen; this is in accordance with the classical views of Thoma regarding the protective function of the intima. This intimal reaction was so well marked in some vessels as to form a new fibro-cellular coat for a weakened artery, the muscle of which had disappeared. This change could not be regarded as due to organization of thrombi. In places the necrosis was so intense and localized that saccular aneurysms developed at the site of the defect, before any intimal thickening could take place. The aneurysms appeared as large cavities lined by a fibrous wall and filled with laminated thrombosed blood clot. At the site of the gap, collections of polymorphonuclear cells had infiltrated in between the meshes of the fibrinous bands. Around the primary aneurysms, smaller secondary aneurysms appeared in local gaps of fibrinoid necrosis. A few scarred areas were noticeable in the kidney and the spleen.

Comment.—Cases of polyarteritis nodosa have not so far been reported in India, while in Europe and America over 350 cases have been reported up to 1940 and between 1940 and 1943 over 200 more cases were recognized (Wilson and Alexander, 1945). This cannot be regarded as due to statistical defect in India, since the acute lesions are too well marked to escape attention in routine autopsies in all the medical colleges in India. The probable conclusion is that the disease is rare in India as compared to Europe and America. It is tempting to think that, in view of the allergic hypothesis first suggested by Gruber (1925) and subsequently emphasized by Berger and Weitz (1938) and the clinical and experimental studies of Klinge (1940), Rich and Gregory (1942, 1943) and others, the lesions would be uncommon in a population where the methods of artificial immunization by the introduction of foreign protein have not advanced to the same extent as in Europe and America. That the arteritis has many points of similarity to the allergic lesions produced in experimental animals gives emphasis to this as the possible ætiological factor. It is noteworthy that in this case the patient had both sulphonamide treatment and injections of horse serum, but this was towards the later stages of his illness. How far the vascular system had been sensitized earlier it is not possible to

decide at this stage from the available history of the case. The intensity and stage of the lesions and some of the early clinical symptoms such as pain in the loin and commencing hæmaturia indicate a developing vascular lesion even when the patient was admitted for malaria. The association with malaria can only be regarded as incidental, since malaria is so common in India and such abnormal vascular reactions have not so far been recognized. The possibility of allergy as a primary ætiological agent in this case is however uncertain, but it is possible that sulphonamide treatment and injections of horse serum may have aggravated a pre-existing vascular lesion. No other atopic or allergic manifestations were evident; there was no eosinophilia in the blood and no history of bronchial asthma. It is noteworthy that Lichtman, Stickney and Kernohan (1943) and Wilson and Alexander (1945) have recorded a history of asthma and eosinophilia as a significant association. A maculo-papular rash is the only feature that could possibly be regarded as allergic.

Histologically the lesions correspond to the stages I and II of Arkin (1930). He describes four stages in the course of the disease, starting with degeneration and œdema followed by an acute inflammatory arteritis progressing on to granulation tissue formation and finally fibrosis and scar formation. The earliest lesion noticed in this case was œdema, followed by a splitting and fragmentation of the elastica prior to the rupture of the elastica described by Dickson (1907) as the earliest noticeable lesion. Grant (1940) has drawn attention to the fibrinoid necrosis as the early lesion. He has also brought out the segmental distribution of the arteritis and its tendency to come up in crops with special involvement of the vessels of the kidney and the heart, features which are well illustrated in this case. Some authors have drawn attention to an association with rheumatism and rheumatic lesions (Friedberg and Gross, 1934; Selye and Pentz, 1943). The histological study in this case has however brought out no lesions that could be regarded as rheumatic. There were no signs of valvulitis, and Aschoff bodies could not be demonstrated in sections of the heart muscle.

Summary

A case of acute polyarteritis nodosa occurring in a patient with malaria is described, and the ætiological relationships of the disease are discussed.

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INTESTINAL FUSO-SPIROCHÆTOSIS

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THE occurrence of spirochætes in the human intestines and fæces has been recorded frequently; some workers such as LeDantec, Broughton Alcock and Sabrazes (Noguchi, 1928) regard the spirochætes as pathogenic and responsible for certain types of dysentery and other ulcerative conditions, but the majority incline to the view that they are only saprophytic commensals. References in the literature to the occurrence of fuso-spirochætes in the intestines seem, however, to be few. Parr (1923) refers to case reports from France and Germany associating the fuso-spirochætal symbiosis with a number of obscure dysenteries, secondary to primary amœbic or other protozoal infection, and suggests that the possibility of its localization in the intestines is worthy of further study. The presence of Vincent's organisms in many healthy mouths, and the generally negative results of animal inoculation experiments have led to the view held by several workers such as Wenyon (1926) that they are purely saprophytic organisms, and that their presence in lesions is accidental. On the other hand, some animal inoculation experiments have yielded positive results, e.g. Kritchewsky and Seguin (Strong, 1942) Strong, Shattuck, Bequaert and Wheeler (Knowles, 1928), E. C. Smith (Hindle, 1931) and others. Knowles (1928) refers to the transient presence of fuso-spirochætes for two or three days in Leishman-stained faecal films taken from cases convalescing after amœbic dysentery.

The four cases reported below seem to be the first on record to show uncomplicated fuso-spirochætosis of the intestines with a characteristic syndrome of diarrhœa and severe pain in the abdomen.

Case 1.—Male, age 35, laboratory assistant. In October 1940 the patient had a sudden attack of severe pain above the umbilicus radiating to the centre of the epigastrium, and diarrhœa with 10 to 12 stools a day. It lasted for 20 days in spite of treatment, then subsided, but recurred after a month and lasted



Fig. 1.—Kidney showing multiple aneurysms of variable size in the cortex and in the boundary zone.



Fig. 2.—Branch of the mesenteric artery showing nodular thickenings along the course of the small branches.



Fig. 3.—Heart showing aneurysmal swellings along the course of the coronary arteries.



Fig. 4.—Liver showing a large aneurysm and scattered small aneurysms in the substance.

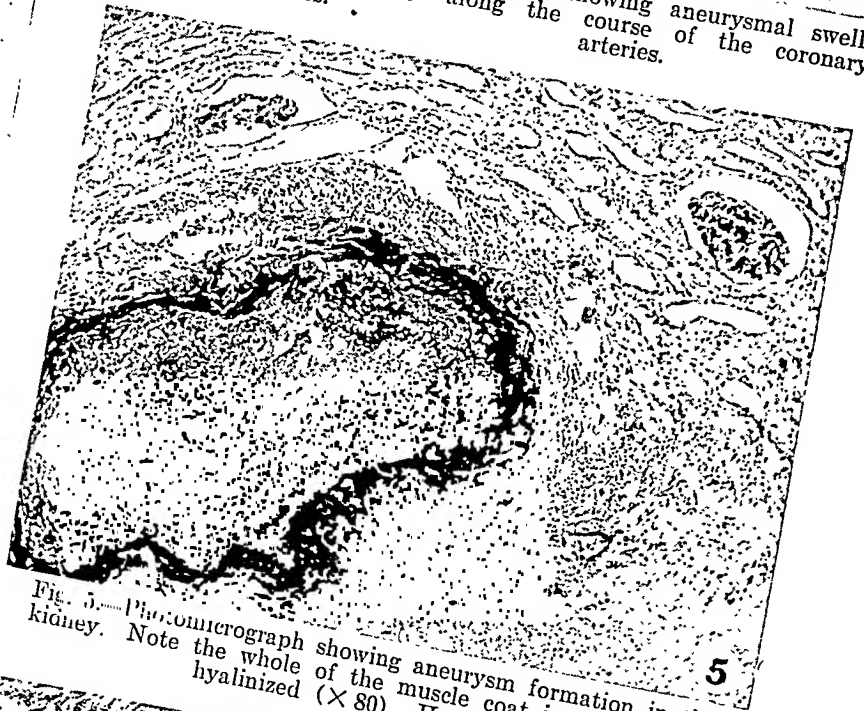


Fig. 5.—Photomicrograph showing aneurysm formation in the kidney. Note the whole of the muscle coat is necrotic and hyalinized (X 80). H. and E.



Fig. 6.—Photomicrograph showing small arteriole in the lung with periarteritis, endarteritis and necrosis of the media and shedding of endothelium of the intima (X 140). H. and E.

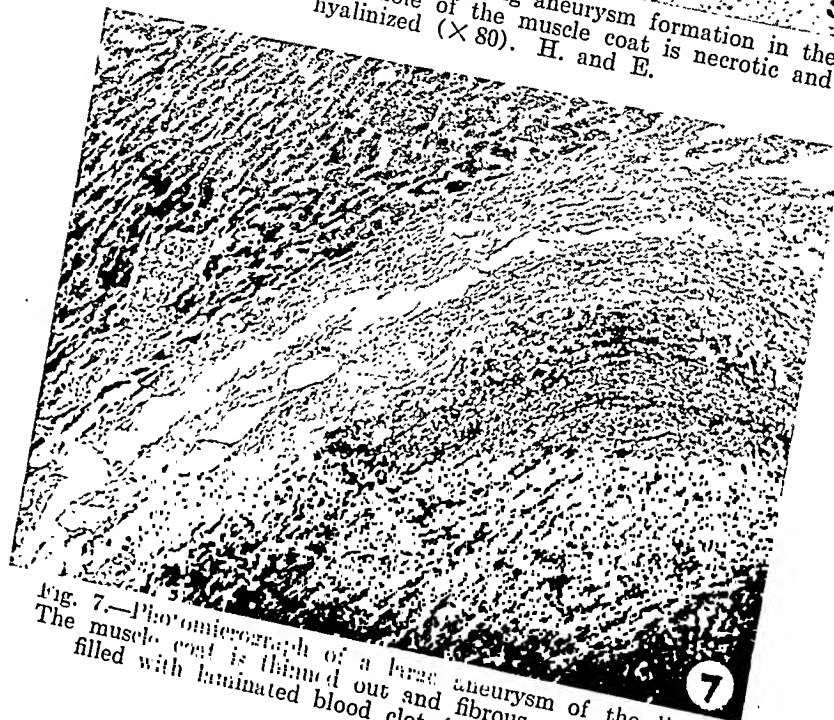


Fig. 7.—Photomicrograph of a large aneurysm of the liver. The muscle coat is thinned out and fibrous and the sac is filled with laminated blood clot (X 80). H. and E.



Fig. 1.—*B. fusiformis*, discrete forms, from faeces of case 2, during acute stage. Leishman. $\times 1,000$.



Fig. 2.—*B. fusiformis*, massed in a clump from same slide. Leishman. $\times 1,000$.

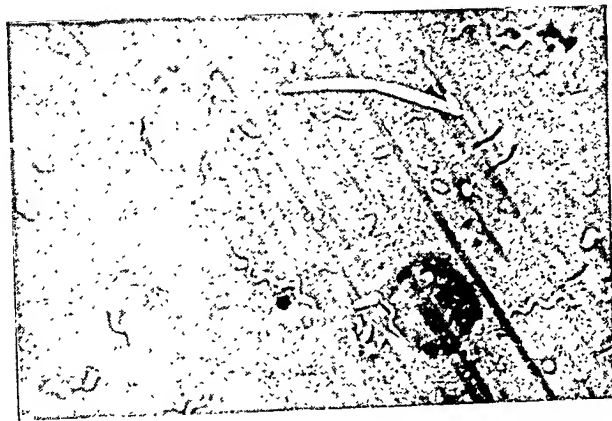


Fig. 3.—*S. vincenti*, discrete forms, from faeces of case 1, during a recurrent attack. Benian's Congo-red. $\times 1,000$.

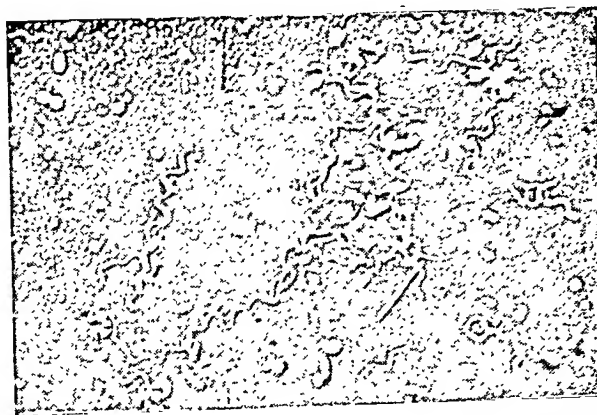


Fig. 4.—*S. vincenti* in groups from same slide. Benian's Congo-red $\times 1,000$.



Fig. 5.—*S. vincenti*, thin forms in one clump, from faeces of case 1, during a recent exacerbation. Benian's Congo-red. $\times 1,000$.



Fig. 6.—*S. vincenti* and *B. fusiformis*, in faeces of case 1, as seen on 27th March, 1945. Leishman. $\times 840$.

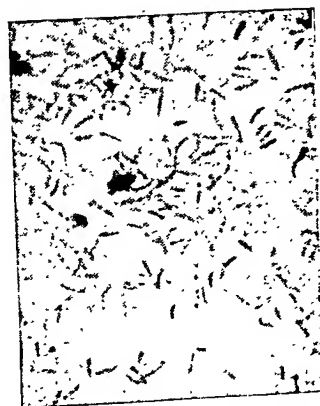


Fig. 7.—'Pink forms' mixed with *B. fusiformis* in faeces of case 2. Leishman. $\times 1,000$.

for another 10 days. Subsequent to this his health has never been as good as before. In June 1943 the patient had typical bacillary dysentery (*B. dysenteriae* Sonne) which responded very promptly to sulphaguanidine tablets. Two months later he had pain in the upper abdomen suggestive of a peptic ulcer; there was no diarrhoea. He was admitted to hospital, and a barium meal showed hyperperistalsis with hypermotility and rapid emptying of the stomach, and constant irregularity of the duodenal cap suggestive of a non-obstructive duodenal lesion. The appendix was visualized, empty within 24 hours. A diagnosis of duodenal ulcer was made and he was treated with aludrox and alkalies, strict dietetic regimen and rest. No improvement was seen. After a month the pain slowly subsided by itself.

On 20th March, 1945, the patient had severe pain in the upper abdomen not relieved by carminatives, etc. Examination showed no rigidity anywhere in the abdomen; tenderness was present midway between the epigastrium and the umbilicus. The pain which had started from above the umbilicus and moved up to the epigastrium, was of unusual severity, increasing to a climax and then easing off slightly. Temperature was normal, pulse 90, tongue clean, no tenesmus. A burning sensation in the eyes and the rectum was present. During the course of that night there were 12 loose and watery stools with mucus but no blood. Repeated examinations of the faeces on subsequent days showed slight cellular exudate but no pathogenic organisms microscopically and culturally. The symptoms persisted in spite of treatment with bismuth and kaolin mixture, castor oil emulsion, sulphaguanidine tablets, etc., and became worse on the 26th night when he had 15 motions. Next morning the stool was examined; a wet saline preparation showed many organisms displaying unusual motility, and a thin emulsion stained with Leishman's stain showed large numbers of spirochaetes and fusiform bacilli in smaller numbers (figure 6, plate XVII). Stovarsol 4 grains was given. The effect was remarkably good. The pain subsided within 2 hours and between 1 and 9 p.m. he had only two motions and none after another stovarsol tablet. The tablets were repeated one twice daily for 2 days more. On 29th March, 1945, and 2nd April, 1945, the stools were normal and spirochaetes very few.

For another two and a half months from this time the symptoms returned with the presence of spirochaetes in stools, and disappeared for a few days with treatment such as stovarsol, carbarsone, nicotinamide, etc. Smears from the gums showed plenty of mouth spirochaetes, *B. fusiformis* and *S. vincenti*. The patient was admitted to hospital and a barium meal was done with practically the same results as before. The Wassermann and Kahn tests were negative. The pH of the saliva was 6.4 to 6.8 and that of the faeces was mostly below 6.6. Proc-

oscopic examination showed no ulceration or other abnormality. Centrifuged deposit of material aspirated from duodenal intubation and stained with Leishman showed *B. fusiformis* in fair number, and *S. vincenti* and mouth spirochaetes in smaller numbers, several polymorphonuclear cells, a few epithelial cells and clumps of gram-positive cocci. Subsequent to this the patient developed a severe exacerbation of pain and diarrhoea, with large numbers of spirochaetes in the faeces. After one injection of bismuth and two of arsenic intramuscularly, the spirochaetes have totally disappeared from the faeces and he has been quite free from symptoms for the last 18 days. He has gained 4 pounds in weight.

Case 2.—Male, age 30 years, animal attendant. On 12th April, 1945, noon, diarrhoea started and till 10 a.m. next day there were 12 stools, loose and watery, preceded by severe griping pain radiating from the umbilicus to the epigastric area. Tenderness over this area present; both iliac fossae free from pain; no temperature; no tenesmus; tongue clean. The faeces showed no cellular exudate, vegetative or encysted forms of *E. histolytica*, Charcot-Leyden crystals or ova of intestinal parasites, but spirochaetes and *B. fusiformis* were present in fair number. Stool culture was negative. The patient was given castor oil mixture 1 oz. thrice daily. Within the next 24 hours he had 20 motions and the pain was of unusual severity. The faeces passed an hour later was greenish in colour and consisted almost entirely of mucus; cellular exudate was marked; Charcot-Leyden crystals were present in large numbers. A wet saline preparation showed enormous numbers of active and motile spirochaetes, but a Leishman-stained slide 2 hours afterwards did not show any spirochaetes, though the wet saline preparation still showed large numbers of spirochaetes with diminished motility 4 to 5 hours after. The Leishman slide showed what appears to be a pure culture of *B. fusiformis* (figures 1 and 2, plate XVII). Certain peculiar forms taking the eosin stain (? spirochaetes) were found in large numbers mixed with *B. fusiformis* in this slide (figure 7, plate XVII). Aerobic culture grew no pathogenic organisms but anaerobic culture in glucose broth grew gram-positive cocci and *B. fusiformis*.

The patient was given stovarsol 4 grains at 12 noon. The pain disappeared and he had an almost normal stool at 4 p.m. Another tablet was given at night. Next day he had one normal motion and no pain, and did not report about his condition till he was sent for. The Wassermann and Kahn tests were negative. The pH of saliva was 6.8 and that of faeces 6.4. The smear from the gums showed mouth spirochaetes, *B. fusiformis* and *S. vincenti*. The faeces on 1st May, 1945, and 7th May, 1945, showed few spirochaetes and on 31st May, 1945, and subsequently no spirochaetes or *B. fusiformis*.

Case 3.—Female, age 32, sister of case 1. She had a severe attack of diarrhoea and pain one year ago, of undetermined aetiology and not responding to treatment, including emetine injections. When she had a bout of diarrhoea, large numbers of spirochaetes and *B. fusiformis* were found in her stools on two occasions; but when she had no diarrhoea the organisms were absent generally, or present in very small numbers. There was no evidence of other infection, microscopically or culturally.

Case 4.—Male, age 45, had a sudden attack of pain around the umbilicus followed by diarrhoea, 10 motions in 12 hours. Microscopical and cultural examination of the faeces gave negative findings, except for large numbers of *B. fusiformis* and spirochaetes, mostly of the type of *S. vincenti* with a few like the mouth spirochaetes or *S. stenogyrate*. Smears from the gums showed various types of spirochaetes and *B. fusiformis*. The condition subsided within 24 hours with castor oil mixture. Subsequent examinations of the faeces revealed no *B. fusiformis* or *S. vincenti* but a few of the type of *S. stenogyrate*.

Incidence of fuso-spirochaetes.—Specimens of faeces of 120 persons were examined, using, in addition to the usual methods, thin, fresh faecal emulsions, air-dried and stained with Leishman's stain. The findings were confirmed by repeated examinations in several cases. The presence of fusc-spirochaetes in the faeces was observed in a total of 16 persons, of which four cases are reported above and 12 are detailed below.

groups of granules taking a deeper stain than the rest of the body and giving them a banded appearance (figures 1 and 2, plate XVII). Measurements are: length 5 to 12 μ , average 8.5 μ ; thickness 0.5 to 1 μ ; pleomorphic forms occur with great variations in size and appearance, both in smears and in anaerobic cultures. The organisms are non-motile and gram-negative and take the Leishman and Giemsa stains satisfactorily. They appear to be identical with Vincent's bacillus, *Fusiformis fusiformis* or *B. fusiformis*.

Spirochaetes.—The predominant type of spirochaete in all the positive cases is morphologically the same (figures 3 to 6, plate XVII). It is a very thin organism with large wavy spirals usually 3 to 5 in number. Measurements were made on spirochaetes in films stained with Leishman's and Benian's Congo-red stains, checked by using Ramsden's filar micrometer and ocular-micrometer on different microscopes, and were compared with measurements on the microphotographs with 1,000 magnification. The length varies from 5 to 20 μ , the most common forms being 8 to 10 μ long, with 3 spirals. The thickness as estimated from that of a bunch of spirochaetes lying close together is about 0.2 μ . The spiral depth is 1 to 1.5 μ and the spiral amplitude or wave length per coil is between 2.5 and 3.5 μ . The spiral amplitude seems to be a more useful and dependable constant for identification of these spirochaetes than the length and number of spirals, both of which vary according to the age and the time of transverse fis-

Case	Clinical condition	Cellular exudate	Other infection	Spirochaetes
1	Pain upper abdomen	Nil	Giardia veg. ++ Ascaris ova +	++
2	Diarrhoea and pain	+	Giardia veg. ++	++
3	Diarrhoea and pain	++ C.L. crystals	Giardia veg. ++	+++
4	Dysentery	+++	<i>E. histolytica</i> veg. ++ Giardia veg. ++	++
5	Dysentery	Nil	<i>E. histolytica</i> veg. ++ Giardia veg. ++	++
6	Dysentery	++	<i>E. histolytica</i> veg. + Giardia veg. ++	+++
7	Dysentery	++ C.L. crystals	<i>E. histolytica</i> veg. +	+++
8	History of old amebic infection ..	++	<i>E. histolytica</i> veg. +	++
9	History of old amebic infection ..	Nil C.L. crystals	Nil	++
10	Chronic dyspepsia	Nil	Nil	++
11	Normal	Nil	Nil	+
12	Normal	Nil	Nil	+

Morphology of the organisms

Fusiform bacilli.—In most of the cases the fusiform bacilli are present in smaller numbers than the spirochaetes except in case 2. The typical organisms have a characteristic shape, thin, with pointed ends, and two, three or more

sion of the organism. Thus it is possible to distinguish the predominant type from other spirochaetes found occasionally in the faeces such as *S. stenogyrate* and the mouth spirochaetes or *S. microdentum*, and *S. mucosum*, whose spiral amplitudes are below 1.5 μ . Of the few types

with a spiral amplitude over 2.5μ , *S. buccalis* or *S. refringens* can be distinguished by its thickness 0.7 to 0.8μ , while *S. eurygyrata* has only 2 coils and is S-shaped and flat. From a detailed study of the morphology and measurements of this organism and its association with *B. fusiformis* it is evident that it is *S. vincenti* (Blanchard), otherwise known as *Treponema* or *Borrelia vincenti*.

Protected by the mucus in the fæces, these spirochætes are found to retain their viability and motility for as long as 6 to 7 hours. The addition of distilled water to the preparation does not cause immobility and plasmolysis later on of the organisms, as noted by other workers. In two preparations made simultaneously, one in saline and the other in distilled water, the spirochætes showed greater motility and for a longer time (5 hours) with distilled water than with saline ($4\frac{1}{2}$ hours). Marked changes in their morphology such as loss of curves, thinning, angularity and granular staining defects were observed when the patient was under treatment with an arsenical like carbarsone.

In the fæces of case 2, large numbers of certain forms taking up the eosin in Leishman's stain were found mixed with *B. fusiformis*. These forms show hardly any structure, look like capsules, and measure on an average $3 \times 0.5\mu$.

Discussion.—From the case reports presented above it will be seen that these organisms grow very satisfactorily in the human intestines under certain conditions. Smears from the gums of these patients showed the presence of fuso-spirochætes. This finding, combined with the observation of Macfie (1917) that the intestinal spirochætes readily withstood the action of artificial gastric juice, suggests that the source of infection is the mouth. The two normal cases at the end of the table may thus be regarded as excreting the spirochætes and *B. fusiformis* through the intestines without developing any lesion. In cases 2 and 4, the organisms develop in the intestines and cause a temporary irritation, possibly due to inflammation or superficial ulceration. In case 1, the conditions present in the intestines are unusually favourable for the organisms and this may account for the chronicity of the symptoms. The likelihood of a classical duodenal ulcer in this case is negated by the irregularity of the onset of pain, the absence of relationship between pain and food, the lack of any relief with the usual dietetic and alkaline treatment, the occurrence of diarrhoea and the repeatedly observed relief with arsenicals. The close parallelism between his symptoms and number of spirochætes in the fæces is suggestive of an ætiological relationship between them.

The duodenum or upper jejunum seems to be the area commonly affected. The location of the pain, the site of tenderness, the absence of tenesmus, the character of the stools, the

frequent association with *Giardia intestinalis*, and the repeated x-ray findings 'suggestive of a duodenal lesion' all lend support to this view. Moreover, the centrifuged deposit of the duodenal intubation material showed a fair number of *B. fusiformis* and a few *S. vincenti* and other mouth spirochætes. Also Ott has recently recorded that out of 13 cases with amœbic ulceration of the large bowels, 6 showed amœbæ in the duodenal contents.

The fact that in a child in this series with fuso-spirochætes and *G. intestinalis*, subsequent to the administration of nicotinamide, amœbic dysentery with more numerous fuso-spirochætes developed, and that the fuso-spirochætes disappeared after two injections of emetine, suggests that fuso-spirochætosis should be regarded as a secondary infection in cases of amœbic dysentery, often clearing up under emetine treatment. It is quite possible that in some of the cases proving resistant to emetine treatment, Vincent's organisms are responsible for keeping up ulceration. The success of arsenical preparations like stovarsol, carbarsone and spirocid in amœbic dysentery may be partly or even entirely due to their action on Vincent's organisms rather than on the amœbæ.

While fuso-spirochætes are so often found in association with amœbic dysentery, they are conspicuously absent in bacillary dysentery. This has been observed also by de Lavergne and Dumont (Parr, *loc. cit.*). It is interesting to remember in this connection that while in amœbic dysentery the reaction of the fæces is generally acid, in bacillary dysentery it is alkaline. Cases 1 and 2, as well as the two normals had fæces with pH values repeatedly below 6.6, while normal healthy persons generally had fæces with pH well over 7.0.

The possibility of Vincent's organisms alone causing a dysenteric state cannot be overlooked in view of Blanchard's experiment (Parr, *loc. cit.*) where he induced a dysenteriform condition in a dog, with spirochætes and fusiform bacilli seen in the motion, by introducing material from a case of Vincent's angina into the digestive tube of the dog. Experimental or accidental transmission of *ulcus tropicum* or Naga sore from man to man has been recorded by Hall Wright, Fox, Apostolides, Pampana and others (Knowles, 1928). These findings, and the constant presence of Vincent's organisms in the lesions, suggest that though primarily existing as saprophytic organisms in the mouth, they can take on a pathogenic rôle and cause ulcerative and gangrenous lesions at several sites in the body. The conditions which bring about a change from the saprophytic to the pathogenic phase are not definitely known. Several factors have been suggested, such as devitalization of tissues by injury or circulatory changes (Strong, 1942), by previous or concurrent infections with other organisms (Knowles, 1928), and by diet deficiencies specially in vitamin B₂ (Clements, James, quoted by Strong).

The possibility of environmental changes in pH, oxygen tension, etc., and the presence or absence of chemical substances acting on the organisms and causing a state of virulence, may explain many of the anomalous findings in clinical and experimental work on this subject.

The place of nicotinic acid in the prevention and treatment of infections with Vincent's organisms is still under discussion. The organisms have been found in abundance in the lesions on the mucous membranes of pellagrous patients (Spies and Butt, 1943), of dogs suffering from canine black tongue, and of pigs with ulceration of the large intestines (King, 1940), and nicotinic acid has quickly eliminated them. But in non-pellagrous conditions with Vincent's organisms, while good results have been claimed by King (*loc. cit.*), Harries and Mitman (1944) and others, many other workers, e.g. Aitken (1943) have not been able to confirm them. In the present series of cases, a temporary advantage was observed in case 1 on nicotinamide treatment; but in the child with fuso-spirochætos and giardia infestation, nicotinamide had no effect on the former, and subsequently the patient developed amœbic dysentery with even more fuso-spirochætes.

Summary and conclusions

1. Fuso-spirochætes have been found in the fæces of 16 out of 120 persons (13.3 per cent). Out of these 16 cases, 4 (3.3 per cent of the whole series and 25 per cent of the fuso-spirochætal cases) show fuso-spirochætes alone, with diarrhoea and pain, two of the more severe cases responding well to treatment with arsenicals. Nine (7.5 per cent of the whole series and 56.25 per cent of the fuso-spirochætal cases) show fuso-spirochætes and a protozoal infection with either *E. histolytica* or *G. intestinalis* or both, with signs and symptoms of the protozoal infection. Two cases (1.6 per cent of the whole series) show a few fuso-spirochætes and a few spirochætes of the *S. stenogyrate* type, without any clinical signs and symptoms.

2. Twenty cases out of 120 (16.6 per cent) including 7 cases with fuso-spirochætes show the presence of spirochætes of the mouth and intestinal type. These figures are lower than those obtained by Parr (*loc. cit.*), viz, 27.7 per cent among 175 healthy subjects and 31 per cent among 193 hospital patients.

3. Out of 7 cases with *E. histolytica* infection, 6 are associated with the presence of fuso-spirochætes, while in 15 cases with *G. intestinalis* infestation, 6 show the concurrent presence of fuso-spirochætes.

4. Out of 13 cases of culturally-positive bacillary dysentery and 6 cases with helminthic infection in the series, none show fuso-spirochætes.

5. The source of infection and the probable site and nature of the lesions produced are discussed.

6. The frequent association between fuso-spirochætes and *G. intestinalis* observed indicates that an investigation of cases of diarrhoea and ulceration of the intestines, with Vincent's organisms in mind, is likely to throw more light upon the ætiology and pathology of some of these obscure conditions.

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(For references please see page 466.)

THE PRESENCE OF RHINOSCLEROMA IN KORAPUT DISTRICT OF SOUTHERN ORISSA

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RHINOSCLEROMA is a rare disease. Its occurrence in India has been recorded by Castellani and Chalmers (1919), De and Chatterjee (1935) and Rao and Menon (1941). Altogether only 8 cases have been reported so far in India. All 6 cases reported by Rao and Menon, came from Ganjam district of Orissa, and the Oriya-speaking tracts of Vizagapatam district of Madras. Koraput adjoins both the localities.

The case under report was observed at Government Headquarters Hospital, Koraput.

Case report

Hindu female, aged 50 years, Oriya Dom by caste, attended the hospital for progressive deformity of the nose and nasal obstruction. She was in fairly good health, quite in keeping with her age and environment. She gave a history of nasal catarrh and obstruction for three years.

Findings.—Anosmia present; nose broadened, thick and flat. A flat circumscribed growth occupied the middle third of the upper lip, extending to the tip of the nose. The margins of the growth slightly raised; the overlying epidermis reddish in colour and markedly thinned out. A small circular area over the tumour, $\frac{1}{2}$ inch in diameter, was denuded of surface epithelium and covered with a thin dry scale. The growth was firm and hard in consistency, painless but slightly tender, and it almost occluded the anterior nares; the interior of the nasal passage could not be examined. No enlargement or tenderness of the regional lymph glands. Clinically no change in neighbouring bones were detected. The soft palate and pillars of the fauces were normal. A good view could not be obtained by with posterior rhinoscopy. Indirect laryngoscopy revealed no abnormality. Blood—Wassermann reaction was negative. A photograph could not be taken.

Clinically the case was diagnosed as rhinoscleroma, and for confirmation, materials from the case were collected and sent to Dr. G. Panja, Professor of Bacteriology and Pathology, School of Tropical Medicine, Calcutta, for favour of necessary examination. The report received from him is reproduced below:

'Material in glycerine saline for culture:—Container found broken and the contents run out. Films of exudate:—Pus cells, scanty fusiform bacilli, gram-

positive cocci in large numbers and gram-negative rod-shaped organisms unlike *B. rhinoscleromatis* found.

'Serum:—Agglutination with a suspension of *B. rhinoscleromatis*—positive 1 in 20 only. Tissue:—On section the epidermis is found intact but thinned. Extensive cellular infiltration is present in the dermis. The cells consist mainly of mononuclear cells and a few large eosinophilic cells. Plasma cells and giant cells are not seen. Mikulicz cells, diagnostic of rhinoscleroma are not found.'

Discussion

Clinical findings of the case are strongly in favour of rhinoscleroma. Moreover her blood serum gave positive agglutination reaction with a suspension of *B. rhinoscleromatis*. The Wassermann reaction is negative. But Klebsiella rhinoscleromatis and Mikulicz cells, diagnostic of rhinoscleroma, were not found on pathological examination. Demonstration of these is only possible in the third stage of the disease. This case may be too early. Complement fixation tests could not be done.

Acknowledgment

I am very grateful to Dr. G. Panja, M.B., D.Bact., F.N.I., Professor of Bacteriology and Pathology, School of Tropical Medicine, Calcutta, for his kindness in examining materials of this case and according his permission for utilization of his report. I am also thankful to Dr. J. N. Das, Civil Surgeon, Koraput, for permitting publication of this report.

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MEPACRINE INTOXICATION AND VITAMIN B DEFICIENCY

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THE occasional development of cerebral excitation and other forms of psychoses in malarial subjects treated with atabrine is the experience of many, and in the past was reported on several times by various workers including Kingsbury (1934), Udalgama (1935) and Hay *et al.* (1935). The exact mechanism of its production is not yet known. Recently the writer came across four such cases of mental derangement.

All four cases had atabrine, a brand of mepacrine, manufactured by Winthrop Chemical Co., U.S.A. These four cases of mental disorder occurred amongst nearly 280 malarial patients treated with this drug.

Case notes

Case 1.—Hindu male, aged 20 years, had fever on 25th October, 1944; blood examination showed a moderate number of *P. vivax* rings and a few schizonts. Treatment as an outpatient with oral atabrine, one tablet (0.1 gm.) at a time—thrice daily, was started on

27th October, 1944, and continued for 5 days. The onset of mental symptoms was on 2nd November, 1944, i.e. one day after the completion of the five-day course of treatment. He was taken as an inpatient on 3rd November, 1944, for the treatment of this complication.

Findings.—Onset of mental symptoms was reported as insidious—restlessness, incoherent and incessant speech, irrational behaviour, confusion, anorexia and insomnia present; occasionally violent. No personal or family history of psychosis is present. There was a yellow coloration of the skin and conjunctivæ; the spleen just palpable; urine examination for detection of atabrine positive; van den Bergh test negative; blood examination showed no malarial parasites. His memory of the period of mental disorder is completely blank.

Signs of vitamin deficiency were present, angular stomatitis and fissuring of tongue with hypertrophic papillæ. On recovery and further questioning he reported burning pain in mouth when spiced food was taken; there was a history of intermittent diarrhoea and flatulence.

Treatment.—Sedatives and intravenous glucose was given daily for nine days with no benefit. On 12th November, 1944, he was given 5 c.cm. whole liver extract (T.C.F.) intramuscularly and nothing else. Next day his mental condition was found better. Two more liver extract injections were repeated on the succeeding days and he was discharged cured.

Subsequent observations.—This patient had three relapses of malaria. Each time *P. vivax* was found on examination of blood. The first and second relapses were treated with oral quinine. During convalescence from the second relapse he was given a regular course of iron and dry yeast extract for three weeks. With this he improved much and gained 12 lb. in his weight and all signs of vitamin deficiency disappeared. In spite of this he had again relapse of malaria on 18th March, 1945, and again scanty parasites were found in his blood.

In this relapse in view of his improved health including freedom from vitamin lack, it was decided to try atabrine again, and find out if state of hypovitaminosis played any part in the development of mental disorder. Accordingly he was allowed to have several bouts of fever till the number of parasites in his blood became moderate. Then atabrine was administered in powdered form, dispensed in cachets, in order to conceal from him the nature of the drug. The daily dose was the same as on the first occasion but the course was extended over 7 consecutive days, the patient being kept under close observation throughout. Beyond slight yellow tinging of the skin nothing untoward occurred. No abnormality was noted in his mental condition.

Case 2.—Hindu male, aged 24 years, jail warder, was admitted into the hospital on 12th November, 1944, for mental derangement.

History.—He had malarial fever due to *P. falciparum* infection and was treated with atabrine, one tablet of 0.1 gm. at a time, thrice daily, in the Jail Hospital. After taking 12 tablets he showed signs of mental disorder, for which he was sent to this hospital.

Findings on admission.—The patient was restless, excited, boisterous, emotional, bursting into peals of laughter without reason; speech incoherent and incessant; irrational behaviour; skin tinged yellowish, test for detection of atabrine in urine positive; spleen just palpable; anaemia present.

Signs of vitamin deficiency.—Patchy atrophic glossitis and scaly dermatitis of scrotum were present. After recovery on questioning it was elicited that he felt burning pain in mouth when spiced food was taken. No irregularity of the bowels and no angular stomatitis.

No family or personal history of psychosis. His memory for the period of mental disorder is completely blank.

Treatment.—Sedatives, and glucose intravenously. After two days his mental condition became normal and he was discharged cured on 14th November, 1944.

Case 3.—Hindu male, aged 35 years, jail warder, was admitted on 30th November, 1944, for mental disorder.

History.—He had malarial fever due to *P. falciparum* infection, for which he was treated with atabrine, one tablet at a time—thrice daily, in the Jail Hospital. On completion of the five-day course, he showed signs of mental derangement for which he was sent to this hospital.

Findings on admission.—The patient was excited, emotional, spontaneously bursting into peals of laughter, restless, talking incoherently and incessantly, behaving irrationally and wandering about aimlessly.

Skin and sclerae tinged yellow; test for detection of atabrine in urine positive; spleen just palpable, only scanty crescents present in peripheral blood; anaemia pronounced.

Signs of vitamin deficiency.—Angular stomatitis; fissured tongue; seborrhoeic dermatitis on either side of nose and along the nasolabial fold. After his recovery further questioning revealed irregularity of bowels, sometimes flatulent diarrhoea, and burning sensation in mouth when spiced food was taken.

No family or personal history of psychoses. He remembers nothing that happened during the period of mental disorder.

Treatment.—Sedatives and intravenous glucose for three days with no benefit. Then 5 c.cm. whole liver extract (T.C.F.) was given intramuscularly. After two injections his mental condition became normal and he was discharged cured on 5th December, 1944.

Case 4.—Hindu female, aged 22 years, had fever on 17th August, 1944, due to *P. falciparum* infection, for which she was given atabrine in doses as in previous cases. After taking 13 tablets she showed signs of mental disorder.

Findings.—The patient was emotional, restless, talked incoherently and incessantly. Her behaviour irrational and immodest. Insomnia and anorexia present. She was very weak, anaemic and emaciated.

Sign of vitamin deficiency.—Pachy atrophic glossitis; a history of long-continued diarrhoea after delivery with spontaneous intermissions; a history of complaint of burning pain on the palms and soles and burning sensation in mouth when taking spiced food.

Treatment.—Thiamin chloride 25 mgm. and nicotinic acid 50 mgm. was injected on 18th August, 1944, at 8 a.m. Next morning unexpectedly her mental condition was found normal. At night she had good sleep and woke up next morning quite refreshed and sane.

Further treatment for about a month for anaemia and vitamin deficiency restored her normal health.

Discussion

A study of clinical notes of the cases shows that all of them were suffering from varying degree of vitamin deficiency, especially deficiency of vitamin B complex. They showed signs of mental derangement on completion of, or towards the end of, a five-day course of atabrine. In no case was the daily dose of three tablets a day for five days exceeded.

The mental disorder of cases 1 and 3 apparently responded favourably to whole liver extract injection, whereas sedatives and eliminants had no appreciable beneficial effect within the period these were given. Seemingly case 4 responded dramatically to parenteral administration of thiamin and nicotinic acid. Case 2 recovered in 2 days with intravenous glucose and sedatives only.

Case 1 in a subsequent relapse, when he was in a good state of nutrition and free from vitamin deficiency, was given atabrine in same daily doses as previously and for a longer

period, i.e. 7 days instead of 5 days. But this time he did not show any sign of mental disorder. Had he any personal intolerance or idiosyncrasy to the drug he would have developed mental derangement, especially when the course was longer and the total quantity given was bigger.

The conditions under which he took the drug on the two occasions were almost identical except the single variation that on the latter occasion he was free from vitamin B deficiency. This fact on superficial examination gives the impression that vitamin B complex plays some part in some in the development of mental disorder in malarial subjects treated with atabrine. Apparent response of cases 1 and 3 to injections of whole liver extract (which contains vitamin B complex) and case 4 to that of thiamin and nicotinic acid lends support to this assumption. On closer examination, however, it is difficult to associate the state of vitamin B deficiency in any way with the aetiology of mental disorder of malarial patients treated with atabrine.

First it is unlikely that such a small quantity of vitamin B (as contained in a few c.cm. of whole liver extract) and in such short periods would have abolished the state of hypovitaminosis B. In fact the objective signs of vitamin deficiency did not disappear. Another point is that in case 2 recovery occurred in 2 days without any vitamin therapy. Possibly the remaining three patients would have recovered without any vitamin, and the liver extract or vitamin injections might not have influenced or contributed in any way towards their recovery. Moreover all cases of mental disorder due to atabrine so far observed were temporary in nature and disappeared with or without sedatives after varying period from a few hours to a few days. This fact also strengthens the belief that vitamin B may not have any curative effect on such psychic disorder.

In case 1, the non-development of mental disorder on the second occasion, when the total dose was bigger and course longer, seems to be significant. It excludes personal intolerance or idiosyncrasy to the drug and gives some ground for the idea that states of vitamin B deficiency may predispose to development of mental disorder in malarial subjects treated with atabrine. But the question arises why only few and not all persons having vitamin B deficiency do develop this mental disorder? To this the reply may be given that personal factors are very variable and so extremely variable results are to be expected. But this reply does not really meet the point.

Whatever may be the rôle of vitamin B (if it plays any rôle at all) in this type of mental disorder in malarial subjects treated with atabrine, to definitely connect it in any way with the aetiology or treatment of this condition, requires extensive study, in which a number of variable factors are to be controlled. The

observations on these cases probably give hints for further investigation.

Summary

Four cases of mental disorder due to atabrine in malarial subjects are reported. In all hypovitaminosis B was present. Mental derangement of two cases apparently responded to injections of whole liver extract (which contains vitamin B) and that of another to nicotinic acid and thiamin. The remaining one recovered with sedatives and glucose. In one case, in a subsequent relapse of malaria, when vitamin B deficiency was no longer present due to previous therapy, as a test, atabrine was given for longer period in same daily doses as before; but this time no mental derangement occurred. A suggestion is made that vitamin B complex deficiency may have predisposing influence on the development of this sort of mental disorder in malarial subjects treated with atabrine.

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A SUGGESTED FIRST-AID TREATMENT FOR COBRA BITE WITH CARBOLIC SOAP SOLUTION

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and

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In studying the effects of surface tension depressants on toxins, Larson and Nelson

(1924) observed that soaps, particularly soaps of unsaturated fatty acids, were capable of detoxifying bacterial toxins and snake venoms. Carmichael (1927) and Cesari and Boquet (1937) working with sodium ricinoleate showed that this soap could neutralize the toxic effects of rattle-snake venom and *Vipera aspis* venom *in vitro*.

The present study deals with *in vivo* experiments on the detoxifying action on cobra venom of various chemical and biological reagents. Of the numerous products tried, the following proved of no value: colloidal solutions of silver, sulphur and iodine; dyes such as methylene blue, fuchsin, gentian violet, crystal violet, Congo red and acriflavine; mucin, agar, milk, olive oil, trypsin, papain, argyrol, hydrogen peroxide, potassium permanganate, and alkaline solutions of pH 8 to pH 9.

Pigeons of 290 g. to 320 g. weight were given a dose of cobra venom in the pectoral muscle. The site was marked and infiltrated immediately afterwards with solutions of the above-mentioned substances. All the pigeons died in 4 to 5 hours, the time normally taken for death to supervene in untreated controls.

On the other hand, similar trials with various soaps proved of undoubted value. Early in the course of these experiments it became evident that carbolic soap (Lifebuoy) was as effective as sodium ricinoleate, and had the added advantage that the local reaction following its infiltration into the tissues was less than that to sodium ricinoleate. As carbolic soap is used in most dispensaries and many homes, special attention has been directed to experiments with this particular soap. Table I shows the results of treatment with 5 per cent emulsion of carbolic soap infiltrated into the site of venom injection in pigeons, *no other treatment being given*.

TABLE I

Number of pigeons	Dose of cobra venom (mg.)	Dose of soap emulsion (c.c.)	Time between venom and treatment (minutes)	Lived	Died
1	0.4	1.0	2	1	..
2	0.4	1.0	90	2	..
1	0.5	1.0	1	1	..
2	0.5	2.5	5	1	..
6	0.5	2.0	10	6	1
3	0.5	1.0	30	2	1 (18 hours).
3	0.5	2.0	30	2	2 (13 and 15 hours).
10	0.5	Nil	30	1	10 (4 hours average).
			(Controls)		

Total treated with soap 18; survived 14. Total not treated 10; survived *nil*.
 Cobra venom 0.4 mg. is a certain lethal dose for pigeons of 290 mg. to 320 mg. weight and will invariably cause death within 12 hours.

From the above it is evident that treatment with carbolic soap will, in a number of cases, save pigeons from certain death, while in other cases the time of death is delayed by several hours. This suggests the value of carbolic soap solution as a useful first-aid treatment pending the administration of antivenene, which, in India, may not be immediately available in rural areas but may be obtained after delay at larger centres. This delaying effect of soap treatment is well brought out in table II. Pigeons were given varying doses of cobra venom and treated with soap 10 minutes later, followed at varying intervals by intravenous administration of 0.25 c.cm. of antivenene (A. V.). More antivenene would of course have saved the pigeons, but the experiment was designed to approximate to village conditions where antivenene if available after a delay of some hours may only be had in limited quantity.

No fixed quantity of the solution can be recommended, as this will obviously depend on the site of the bite, but as much as can conveniently be given, say 5 c.cm. should be given. A crucial incision, preferably with a razor blade, should then be made to encourage free bleeding. In no case should the wound be rubbed with crystals of potassium permanganate. In our opinion the use of potassium permanganate in the local treatment of snake bite is of no value. Apart from this, amputation following cellulitis, sloughing, gangrene, etc., may be necessary after the use of this reagent, which should therefore be avoided.

Two and a half c.cm. of carbolic soap solution injected intramuscularly into pigeons has never given rise to necrosis. Five c.cm. injected subcutaneously into a goat caused erythema and swelling lasting about 4 days but no untoward effects followed. One c.cm. of a 10 per cent solution infiltrated into human

TABLE II

Treatment	Number of pigeons	Dose of venom (mg.)	Interval between venom and antivenene (minutes)	RESULT	
				Survived	Died
Soap plus antivenene ..	2	0.5	90	2	..
Antivenene only ..	2	0.5	90	1	1
Soap plus antivenene ..	2	0.5	120	2	..
Antivenene only ..	2	0.5	120	1	1
Soap plus antivenene ..	3	0.6	120	3	..
Antivenene only ..	3	0.6	120	2	1
Soap plus antivenene ..	3	0.6	15	3	..
Antivenene only ..	3	0.6	15	2	1
Soap plus antivenene ..	3	0.8	15	3	..
Antivenene only ..	2	0.8	15	..	2
Soap plus antivenene ..	3	1.0	15	2	1
Antivenene only ..	2	1.0	15	..	2
Soap plus antivenene ..	1	1.2	15	..	1
Antivenene only ..	1	1.2	15	..	1

Total treated with soap plus antivenene 17; survived 15. Total treated with antivenene only 15; survived 6.

In view of these results, the use of a 5 per cent solution of carbolic soap as a first-aid treatment in case of cobra bite is suggested. This solution should be kept ready for use in all dispensaries along with a sterile 10-c.c. syringe. The solution may 'gel' on standing but readily re-dissolves when gently heated. In the event of a cobra bite, a tourniquet should be applied as usual over a single bone, e.g. in the case of a finger bite it should be applied around the base of the finger and a second tourniquet above the elbow, or in case of a bite on a toe, one tourniquet applied around the base of the toe and the second above the knee. Soap solution should then be infiltrated into the site of the bite. The solution should be injected around the fang-marks, about 0.5 c.cm. to 1 c.cm. being given at various points so as to completely surround and infiltrate the site of the bite. It should also be injected at various depths to a maximum of half an inch.

volunteers caused slight burning pain lasting about 20 minutes followed by redness, swelling and induration but no inconvenience was experienced after the first hour or two.

The authors will be grateful for any reports of cases treated on the above suggested lines. Such reports should contain the following information:—

(a) Was the snake definitely identified as a cobra?

(b) Site and details of bite.

(c) Interval elapsing between bite and injection of soap solution.

(d) Quantity of soap solution injected.

(e) Antivenene (including period after bite at which serum was given; dosage and whether administration was intravenous).

(f) Other details with regard to local reaction, symptoms and progress of the case.

It is emphasized that soap is *only* a first-aid treatment to be used for local infiltration only

and must be considered as an adjuvant to treatment with antivenene. *On no account should soap be given intravenously as a substitute for antivenene.*

Similar experiments with viperine venoms are in progress.

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A Mirror of Hospital Practice

A CASE OF SEPTICÆMIA TREATED WITH PENICILLIN AFTER FAILURE OF SULPHONAMIDE THERAPY

By R. N. CHAUDHURI, M.B., M.R.C.P. (Edin.),
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and

S. M. GHOSH, M.B.

(From the School of Tropical Medicine, Calcutta)

ALTHOUGH the uses, doses and methods of administration of penicillin have now been well outlined according to our present knowledge of the subject, doubts may arise in practice when perhaps it may be wise to follow one's clinical judgment and not to too strictly follow the rules. In this connection, sufficient interest attaches to the following case to justify a report being published.

Case report

A doctor had been well until the 12th August, 1944, when he felt a sharp pricking pain on the left nipple, while undressing. On examination, he noticed a small pimple in the area, but took no notice of it. The pimple gradually became bigger in size and slightly painful. On the 14th, he felt feverish and pain on movement of the left arm but went to work as usual. Two days later, there was a sharp rise of temperature with chill, headache and pains in the body, and he took to bed.

On examination.—A thin-built man. Temperature 104°F., pulse rate 80 and respiration 20 per minute; tongue coated. A furuncle was seen on the left nipple with a chain of small discrete, movable and tender glands in the left axilla. There was no other significant finding on clinical examination.

Laboratory findings.—Blood examination repeatedly showed no malaria parasites. The white cell count was 6,500 per c.mm. with 82.5 per cent polymorphonuclear cells. The blood as well as the discharge from the pimple grew no organisms. The urine showed a trace of albumin with scanty pus cells and a few red cells. Results of subsequent examinations are shown in the table below:—

Date	White cell count	Blood culture	Agglutination test	Urine	Stool	Pimple smear
19th August ..	8,400 with 79% polymorphs.	Sterile	Widal negative.	Scanty pus cells.
25th ..	6,050 with 88% polymorphs.	"	Widal and Weil-Felix negative.	Albumin trace. Few pus cells.	Negative	..
30th ..	9,400 with 80% polymorphs.	..	Do.

Diagnosis.—Malaria having been excluded, dengue and enteric were suspected owing to bradycardia, but in view of the history and the local lesion, a clinical diagnosis of staphylococcal septicæmia was made.

Treatment and course.—On the 17th August, the patient was put on sulphathiazole by mouth with hot compresses of 1 in 1,000 acriflavin solution applied locally. He was also given palliative treatment including intravenous glucose with vitamin C, etc. After administration of 9 grammes of sulphathiazole in three days, his headache became worse, he felt sick and complained of abdominal discomfort; the drug was then discontinued. During the next two days, his condition seemed to deteriorate, and on the 22nd a suggestion was made to try penicillin, but no genuine preparation being available sulphadiazine was started instead. A total of 28 grammes of this drug were given in five days but without any effect.

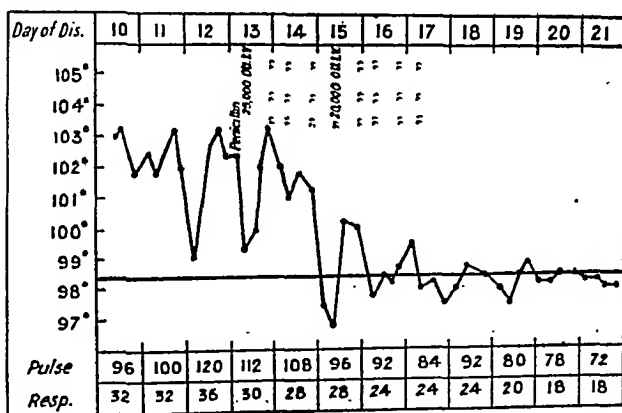
In the meantime, the patient's condition was getting worse. He became restless, complaining of severe headache practically all the time. The temperature was of high remittent type with repeated rigors, but the pulse was relatively slow and respiration slightly increased. Blood pressure 110/65 mm. of mercury. The face was puffy; the tongue red and dry. He was constipated with a distended abdomen, but the urinary output was fairly good. The furuncle and axillary glands remained practically the same as before. About this time, he complained of slight pain in the scrotum which was found to be due to local dermatitis and swollen and tender testes (left).

The patient was now seriously ill, causing anxiety. He was seen by several doctors including a surgeon in consultation, and our only hope seemed to rest on penicillin which had hitherto been unobtainable. After much enquiry and search we managed to secure only one ampoule (100,000 units) and this treatment was started on the 26th August, it being given intravenously twice daily, in doses of 25,000 units each. With these four doses, the temperature dropped to sub-normal (*vide chart*) in the morning of the 28th, and the patient felt better. Fortunately, another ampoule could now be obtained, so that treatment was continued for a further three days (20,000 units b.d.). Convalescence started rapidly and was uneventful.

Discussion

It is very likely from a clinical standpoint that we were dealing with a case of staphy-

lococcal septicæmia following a self-inflicted trauma to a furuncle on the nipple. Prior to the advent of sulphonamides, reports of cure from this disease were rare, but with their introduction isolated cases of recovery began to appear. Now with penicillin we have a powerful weapon to combat this condition. The method of treatment with this drug is rather arduous for doctors with limited facilities as in private practice and disagreeable to the patient if continued for several days. It has been recommended that for systemic infection penicillin should be used after making bacteriological diagnosis and given in adequate doses at 3 to 4 hourly intervals (or by the drip method) so as to maintain the proper blood concentration. In the present case, blood was cultured twice (while the patient was having sulpha drugs), and the results were negative. Yet it was decided to try penicillin on clinical grounds, and this seems to have been justified by the end results. Frequent administration was however not possible. Nevertheless, the improvement after four doses in two days was dramatic.



Temperature chart.

During the course of the illness, the patient's tongue became raw and there was scrotal dermatitis with tender swelling of one testes. Although the exact cause of these manifestations is not clear, it is possible that they were caused by the administration of sulphonamides in large doses thus interfering with the biosynthesis of riboflavin in the intestine, while the body requirements must have been increased owing to a heavy infection. Incidentally, one fact worth mentioning is that the patient while under sulpha treatment passed unchanged a few tablets of sulphadiazine in the stools due to failure of one of the nurses in attendance to crush them before administration. It is well to impress the importance of this simple, but apt to be neglected, routine on the attendants.

Conclusion

A doctor with acute septicæmia made a rapid and complete recovery when treated with penicillin after showing no response to sulphonamide therapy. The turning point of the illness in the

critical stage was undoubtedly due to penicillin treatment, although the diagnosis was not confirmed bacteriologically and the drug was administered infrequently owing to the difficulty in obtaining a sufficient supply. As penicillin is available now in civil practice, the latter difficulty may no longer arise, but a negative bacteriological report should not outweigh a definite clinical diagnosis and indications for its use.

Acknowledgment

So many people were directly and indirectly responsible for assistance in this case that it is impossible to mention them here individually, but we take this opportunity to express our sincere thanks to all of them.

TWO CASES OF STRANGULATED HERNIA

By A. SWARUP,

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Case 1.—R. S., 42 years, was admitted to hospital on 5th February, 1944, with a large mass in the right scrotal region which extended up to the groin, fully occupying the inguinal canal. He came walking and was not in great distress. The abdomen was not distended, nor was there any history of retention of urine or of constipation. The only thing he complained of was discomfort and some pain due to the swelling.

The history he gave was that two years back he was operated on for hydrocele on both sides, and ever since then he had been suffering from hernia of the right side. It had been reducible, but some 15 days ago, it had descended and since then it had been in its present condition and could not be reduced. As it was causing some discomfort he went to a branch dispensary where he remained for a week, but finding no relief he came to the sadar hospital.

Under chloroform anaesthesia an incision for radical cure of hernia was made, but upon opening the sac it was found to contain some two feet of ileum and its mesentery. The ileum was blue and cedematous and the mesentery was thickened to the size of almost an impregnated broad ligament. An attempt was made to reduce the mass back to the abdominal cavity, but in doing so the ileum gave way in two places and faecal matter poured out of it in the field of operation. This was mopped clean and the piece of gut which had ruptured was excised and an end-to-end anastomosis was made. About a foot of the ileum with mesentery had to be removed. The bleeding from the cut mesentery gave some trouble, but ultimately was controlled. After resection, the herniated mass could easily be reduced back into the abdominal cavity. The operation was then completed in the usual way. Before sending the patient from the operation room 5 c.cm. of soluble sulphonamide and $\frac{1}{4}$ grain of morphia were given by injection.

During the first three days the treatment consisted in giving saline per rectum by drip method and glucose and soda solution sips by mouth and keeping the patient in Fowler's position. Soluble sulphonamide was repeated thrice but later replaced by sulphonamide by mouth. On the fourth day his bowels moved, and he began to feel hungry.

Case 2.—Hindu male child, aged nine months, was brought to hospital on 20th January, 1945, by his mother for strangulated right inguinal hernia. The history was that the child had been suffering from hernia since his birth but for the last 3 days it had not gone back. His abdomen was distended and tense, and he was vomiting. He had passed neither flatus nor faeces for 3 days. The general condition was fair. He was prepared for operation, and under chloroform and ether anaesthesia, the sac was opened when both caecum and ileum with the appendix were found in it. At this moment the child stopped breathing and artificial respiration had to be performed. Soon the breathing was restored, and an attempt to reduce the contents of the sac into the abdomen was made, but the gut gave way, and a purse-string suture had to be applied to the ruptured intestine. Eventually the contents were put back into the abdominal cavity and the wound closed and dressed. An intramuscular injection of soluble sulphonamide was given and the child sent back to the ward. For the first 24 hours he did not pass flatus, the abdomen became distended and his condition caused anxiety. After 24 hours the sulphonamide was repeated and turpentine stupes were applied to the abdomen. After this the child had a motion, when the distension of the abdomen became less. Next day, another motion was passed. His recovery now became rapid and on the 8th day the stitches were removed and he was discharged cured on 29th January, 1945.

NITRITOID CRISES AFTER INTRAVENOUS INJECTIONS

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ACUTE vasoparetic reaction or nitritoid crisis is a term employed by Milton to express the symptoms and lesions resembling those of amyl nitrite inhalation produced after the intravenous injection of substances like organic and pentavalent compounds of arsenic and antimony. The following cases are of interest in this connection:—

The intravenous injection of urea stibamine 0.05 gm. (Union Drug Co.) in a strongly-built adult suffering from kala-azar ended fatally. The patient showed all the symptoms of anaphylactoid shock, *viz.* constriction and swelling of the throat, face, and lips with cyanosis and rapid fall of blood pressure followed by deep and stertorous breathing, coma and finally death; all within 15 to 20 minutes in spite of my best efforts to rescue

him. This was the first urea stibamine injection which the patient had received, and death might possibly have been due to over-sensitiveness (opinion of Dr. S. K. Sen, Civil Surgeon, Purnea). It will not be out of place to mention here that during the course of more than 20 years of hospital practice I have given not less than 20 to 30 thousand intravenous injections and I had seen many cases even with severe reactions but none ending fatally.

Another case of intravenous antivenom injection showed similar symptoms particularly cyanosis. It was an advanced case of snake bite poisoning with involuntary dribbling of saliva, loss of consciousness and loss of reflexes. Immediately after the intravenous injection the patient developed cyanosis and died.

It is not known why anaphylaxis and anaphylactoid shock occur in some persons and not in others and why not generally after the 1st injection but usually after the 5th or 6th injection even when the dose is not increased. Reactions are said to be more common in cases with thyroid disturbance. Liver dysfunction is also found responsible for this reaction inasmuch as it has proteopexic and detoxicating functions. Acidosis is also a factor for producing this reaction.

Injection of adrenaline chloride as a routine before all intravenous injections is probably the best measure to avert critical reactions. Glucose oral, 2 or 3 hours before the injection, should always be given to protect the liver cells from the toxic effects of the drug. Rest before and after the injection is necessary. No solid food should be taken for some hours (6 to 8) before the injection. To treat serum reaction, calcium is a drug of choice.

SULPHONAMIDE THERAPY IN SEPTIC CÆSAREAN SECTION

A CASE REPORT

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and

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A MOHAMMEDAN female, aged 23, a dwarf belonging to a family of dwarfs, primigravida, full-term, was admitted into hospital on 5th February, 1945, at 10-30 a.m. with obstructed labour for three days. A number of country dais had tried to deliver her at home.

On admission, her general condition was found very low, with generalized oedema and occasional rigors. The vulva was swollen and lacerated with an offensive discharge. The bladder was distended; urine was drawn off and was found loaded with albumin. Blood pressure 160/100; temperature 100°F., pulse feeble. Recuperative treatment with intravenous glucose, calcium gluconate, morphia and rest was given after an enema. At 3-30 p.m. the patient had sufficiently recuperated to permit an examination. The uterus was still found in tonic contraction, and fetal heart sounds were not heard. Pelvimetry showed the interspinous diameter 8 inches; intercrystal 8½ inches, external conjugate 6 inches; the pubic arch widened; transverse diameter of the outlet hardly admitted three interphalangeal knuckles between the two tubera ischii;

vaginal walls lacerated, membranes absent, os fully dilated, a big caput present, head high and jammed at the inlet.

In view of the degree and nature of the pelvic contraction, a classical Cæsarean section was risked in spite of sepsis and threatening eclampsia. On opening the abdomen, evidence of commencing peritonitis was found. Incision of the uterus was followed by the escape of gas from inside. The foetus and membranes were removed in a state of decomposition. Sulphonamide powder was introduced into the uterine cavity before closing it, and soluseptasine 10 c.cm. was injected into the peritoneal cavity. The omentum was tucked behind the uterus, and the abdomen was closed in layers after ligation of the fallopian tubes.

The temperature touched normal next morning and the patient remained well till the third day when the blood pressure was 120/80. The general peritoneal cavity remained unaffected throughout, but pelvic peritonitis with cellulitis insidiously developed giving rise to fever and maintaining a low fluctuating temperature for the next seven days. The lower stitches gave way, and the wound gaped exposing part of the uterus. No interference was made except change of dressings. Thiazamide (M&B 760), 6 tablets a day, was given for three days. The abdominal wound slowly healed by second intention and the patient was discharged cured on 25th March. The lochia were normal throughout.

Discussion

Forcible delivery with craniotomy with evisceration and piece-meal removal of foetal parts usually leads to serious damage to the birth canal. Even if the patient escapes from septicæmia, a nasty sloughing of the vagina and cervix occurs, and pelvic cellulitis and even peritonitis may follow. The patient may die from exhaustion. Or perhaps she falls a victim to chronic invalidism throughout life. In our case this type of interference, in the presence of such a high degree of sepsis and devitalization, would have been disastrous. On the other hand a frankly septic uterus usually contraindicates delivery by the abdominal route. In this case, both the adverse conditions were present. In these embarrassing circumstances, the easiest and the quickest method of relief, namely a classical Cæsarean section, was undertaken with unexpectedly happy results. Lower uterine segment Cæsarean section was considered difficult, and Cæsarean hysterectomy risky. Porte's Cæsarean section with exteriorization of the uterus is neither difficult nor risky, but it is not very commonly practised.

Although peritonitis had set in before the operation, post-operative peritonitis did not occur, probably for the following reasons: (a) Introduction of soluseptasine into abdominal cavity. (b) Shutting off of the general peritoneal cavity from the source of sepsis by placing the omentum behind the uterus. Puerperal endometritis did not occur as there was enough sulphonamide powder in the uterine cavity to eliminate most of the organisms. Local sulphonamide therapy was reinforced by the oral administration of thiazamide which prevented further extension of the infective processes.

All these, however, did not prevent pelvic peritonitis and pelvic cellulitis, probably for the following reasons: (a) The infective organisms which had penetrated the myometrium and lodged in the parametrium could not be influenced. It may also be that some of the organisms were not sensitive to sulfa drugs. (b) Contamination of pelvic peritoneum during the removal of septic materials from the uterine cavity. (c) Insufficiency of soluseptasine for the pelvic cavity which was most infected. (d) Probably oozing of septic discharges from the uterine cavity during uterine involution.

It must, however, be recognized that this may be one of the few and exceptional cases of success. How much did her recovery owe to the fact that the infective organisms were sulfa-sensitive? One cannot find out beforehand whether in a particular case the organisms are sulfa-sensitive. This is particularly so in an institution where facilities do not exist for detailed bacteriological investigations.

Acknowledgment

We are grateful to Major G. B. Thomas, Superintendent of the Government Hospital for Women and Children, Egmore, Madras, and Professor of Obstetrics and Gynaecology, Madras Medical College, for valuable comments and suggestions on this paper.

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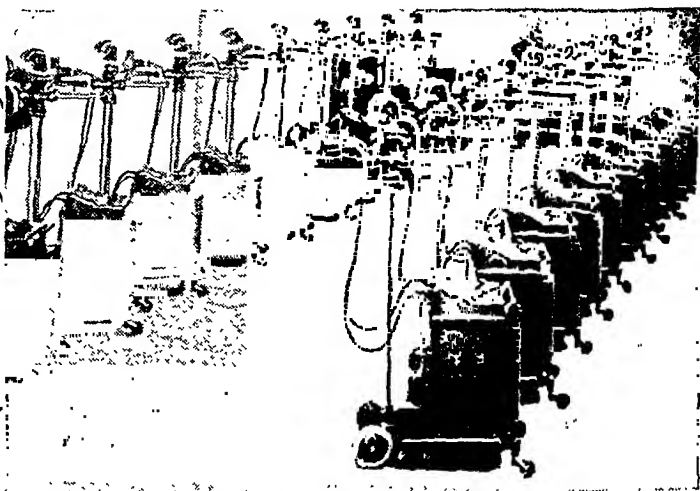
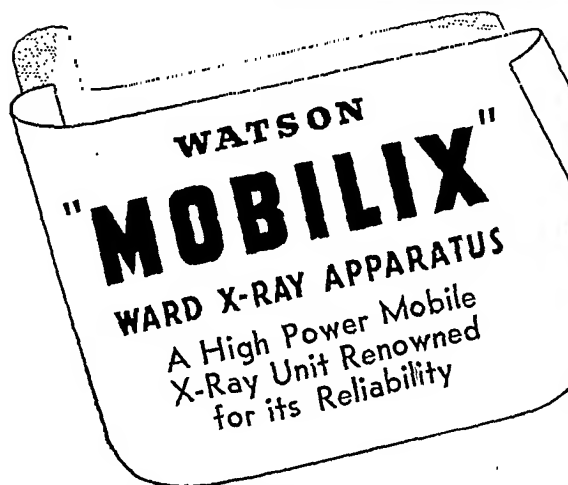
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Indian Medical Gazette

SEPTEMBER

JAUNDICE AND OTHER DISEASES TRANSMITTED BY NEEDLES AND SYRINGES

DURING recent years, certain outbreaks of jaundice have attracted much attention. In many parts of the world, outbreaks of infective hepatitis have been seen, and in India this disease has been very common in certain areas in both civil and military population. The ætiology and pathology of this condition have been closely studied, and much evidence has been accumulated to indicate that it is a virus infection, that the virus is circulating in the blood, and that by the injection of serum taken from patients it is possible to transmit the disease experimentally to volunteers. This condition of infective hepatitis was discussed in this journal (March 1943, p. 153).

Another interesting event was the occurrence of no less than 28,000 cases of jaundice in men in the American army after yellow fever vaccination with certain batches of yellow fever vaccine during the early part of 1942. It is believed that the infection was traced to the human serum used in making the vaccine. When this was discovered, the cessation of the use of human serum in making the vaccine was followed by the disappearance of this jaundice after yellow fever vaccination.

Certain other outbreaks of jaundice have been recorded during recent years. Recently Droller in the *B. M. J.* recorded the occurrence of 62 cases of jaundice in 450 patients attending a diabetic clinic, and the investigation of these cases indicated that the jaundice was probably caused by inadequate sterilization of syringes and needles in use in the diabetic clinic, needles or syringes being infected probably with the virus from one or more of the patients, and the virus being introduced into other patients during the taking of blood from a vein in the clinic. Similar outbreaks of jaundice have occurred from time to time in venereal disease clinics, and have probably been produced in the same way, traces of blood being left in the needles or syringes containing the virus, and subsequent sterilization being inadequate to destroy the virus.

In certain clinics, actual tests were made with the methods of sterilization in use and it was found that they were inadequate to destroy the infective agent. This jaundice, which has often been attributed to the administration of arsenic in venereal disease clinics and has been called post-arsenical or post-arsphenamine jaundice, has been almost eliminated in certain centres by the adequate sterilization of needles and syringes.

Similar outbreaks of jaundice have been recorded in clinics and institutions where the taking

of blood for certain tests and the giving of injections have been a routine procedure. In addition to diabetic clinics, clinics for rheumatism, and tuberculosis sanatoria have recorded such outbreaks. Moreover, considerable evidence has been seen in certain areas that serum and plasma transfusions used in various conditions, particularly for war injuries, have been followed in appreciable number of cases by the occurrence of jaundice, and figures as high as 10 per cent for the incidence of jaundice following such transfusions have been given. It now seems possible, if not probable, that in infective hepatitis, jaundice occurring after yellow fever vaccination, post-arsenical jaundice and jaundice seen in special clinics and institutions are probably all of a similar nature and are caused by a virus or group of viruses.

It has actually been shown in post-arsphenamine jaundice that the virus can be isolated from the blood which, injected into a healthy person, can cause jaundice. Similar findings were made in the cases following yellow fever vaccination. Moreover it has recently been shown that in some patients showing no sign of illness or jaundice the similar virus can be found in the circulating blood. These facts considered together give a reasonable explanation of these extraordinary outbreaks which have been recorded in recent years in certain medical centres, and give a clear indication as to how these outbreaks can be prevented.

Practically all these findings have been recorded in England and in America, though a similar report has been made in Scandinavia. We have however no reason whatever to doubt that jaundice caused in this way by infected needles and syringes can occur and has occurred in India. One has only to see the extremely inefficient methods of sterilization of needles and syringes used in some hospitals and clinics in this country to understand how conditions here are very favourable for the occurrence of such outbreaks of jaundice.

During the war, syringes and needles of good quality have been difficult to secure. While some attempt has been made to sterilize needles, little or no attempt has often been made to sterilize syringes properly. During sterilization, syringes are frequently cracked or broken and rendered useless; they have been very difficult to replace, so that risks of breakage have been reduced to a minimum by the adoption of methods of sterilization which recently have been shown to be completely ineffective.

It is easy to understand how needles and syringes can be contaminated during the process of drawing blood from a patient's vein. Until recently however it has not been realized that a contaminated syringe used for withdrawing blood from a patient's vein can infect the blood of that patient. A recent study published in the *B. M. J.* by Mendelsohn and Witts demonstrates this fact, and the taking of

samples of blood for blood-sugar estimation was thus able to cause an outbreak of jaundice in a diabetic clinic.

'When blood is taken from a vein with a syringe by the orthodox technique some of the blood is sucked back into the vein when the tourniquet is released. If, therefore, the syringe is not sterile the patient is exposed to infection.'

It will thus be seen how the sterilization of needles and syringes is a matter of vital importance. So important has it been that the Medical Research Council of Great Britain has made a special study of this matter and published a memorandum on the subject written by a special committee of ten well-known bacteriologists and research workers*. This memorandum repays close study by all medical men.

The memorandum starts with an introduction stressing the great variety of infections which have been transmitted through faulty sterilization of needles and syringes. Such conditions include streptococcal cellulitis, streptococcal and staphylococcal infections, tuberculosis, meningitis, tetanus, gas gangrene, infective hepatitis, and malaria. The introduction states that in hospitals and clinics where injections are numerous, entirely safe methods are easily practicable and ought to be used and taught; in very few hospitals and clinics are the recommendations of this memorandum properly carried out at the present time. The following are extracts from the memorandum.

'Complete bacteriological sterility can be achieved only by sterilization in the autoclave or hot air oven. Boiling in water will destroy all pathogenic bacteria except those that produce resistant spores. Boiling in water to which a little sodium carbonate has been added will kill spores as well as non-sporing bacteria, but cannot be recommended as a method for sterilizing syringes, because the residual alkalinity of the syringe may destroy certain of the drugs and biological products to be injected. Chemical disinfectants, including alcohol, if they kill spores at all, do so very slowly, and cannot always be relied upon to destroy even non-sporing bacteria in syringes. Since incidents due to spore-bearing bacteria have proved rare, a boiled syringe may be accepted as reasonably safe where sterilization in the autoclave or hot air oven is impracticable, but a boiled syringe is not necessarily sterile, and its safety cannot be absolutely guaranteed.'

'A fresh sterile syringe and needle must be used for each injection or aspiration. In clinics where many injections of the same fluid are given, the same syringe may be used for several consecutive subcutaneous or intramuscular—but not intravenous—injections, provided that a fresh needle is used for each patient.'

'A syringe that has been used for aspiration, e.g. of blood from a vein, or pus from an abscess, or for intravenous injection, which always entails aspiration of blood, must be cleaned and sterilized before it is used again. It is essential to keep syringes for injection separate from those used for aspiration.'

'Syringes and needles require thorough cleaning after use, before re-sterilization. Sterilization methods may be unreliable if the syringe or needle contains dirt or coagulable protein. Needles must be kept sharp.'

'Handle needles with sterile forceps only, syringes with dry, washed hands, taking care to touch only

the outside of the barrel and the handle of the piston. Do not talk, cough or sneeze over a sterile syringe. Do not allow a sterile needle to touch any unsterilized surface or object before use.'

'Persons with known or suspected upper respiratory infections must wear impervious masks while carrying out inoculations or injections.'

'The operator and all assistants must wash their hands thoroughly with soap and warm water and dry them on a clean towel before commencing work, and at intervals during prolonged operations. As an extra precaution during mass inoculations, or if there is reason to think that the operator's hands are infected, the hands may be steeped in some suitable disinfectant, such as hypochlorite solution containing at least 0.1 per cent of free chlorine.'

'Use of a pocket handkerchief must at once be followed by a thorough hand washing.'

'The practice of "dishing up" a sterile syringe and needle in an open bowl, especially one which contains any liquid, is to be unreservedly condemned. Sterile syringes and needles must be placed in sterile covered containers.'

'*Rinsing the sterile syringe in contaminated "sterile" water or saline.*—Use dry-sterilized syringes whenever possible. If wet-sterilized syringes are used, and need rinsing in sterile saline, the saline for the purpose must be taken directly from a previously unopened, autoclaved bottle. After opening, the saline bottle must be discarded, and not kept for future use. To remove the risk that saline bottles, once opened, will be kept and used again, it is advisable to have saline autoclaved in small quantities, say 10 or 20 ml., for the purpose of rinsing syringes.'

'*Intrathecal aspirations and injections.*—Needles, syringes and manometers for intrathecal work need specially careful sterilization. Hot air sterilization should be used when practicable; otherwise, sterilize by autoclaving or by boiling for five minutes.'

Contamination of injection fluids

'Vaccines, diphtheria toxoid, and other prophylactic agents which contain a disinfectant such as phenol, are commonly dispensed in rubber-capped bottles. These may be kept for repeated use provided that due care is taken to sterilize the cap each time before puncturing it, and to preserve its integrity.'

'As far as possible, for isolated injections at intervals, single dose containers should be used.'

'Rubber-capped vaccine bottles, particularly by bakelite studded caps containing an absorbent pad impregnated with 10 per cent solution of chloroxylenol are strongly recommended.'

'Older patterns of vaccine bottle have rubber caps which are unprotected, and which must be sterilized before puncturing. The best way to sterilize them is to wipe them with a clean lint swab dipped in tincture of iodine or 75 per cent v/v alcohol.'

'It is unwise to puncture one cap too frequently because small leaks may then develop through which contamination can enter.'

'To cleanse the skin before the injection, rub the selected inoculation site with a small quantity of spirit or tincture of iodine on a lint swab, and allow to dry.'

The choice of syringes and needles

'All-glass syringes are easier to clean and sterilize than are those made of glass and metal. They are less likely to break on heating, and they have no cement to melt in the oven or autoclave. If properly cleaned and lubricated, they may be assembled before sterilization.'

'The only advantage of the glass-metal syringe is its less fragile nozzle. It is more difficult to clean, and it is apt to break on heating, because of the unequal expansion of the glass and metal; moreover, the cement will melt in the hot air oven and may do so in the autoclave.'

Detailed instructions are given regarding the sterilization of all-glass syringes.

* Medical Research Council War Memorandum No. 15. *The sterilization, use and care of syringes.* 1945. His Majesty's Stationery Office, London. Price, 4d. net.

New syringes should be assembled, lubricated and cleaned, and then fitted in a test tube wrapped in paper (fig. 1) and dry sterilized. For syringes which have been used it is recommended that they should be washed out with an antiseptic immediately after use, 2 per cent lysol being suggested. The syringe and needle should then be thoroughly cleaned with tepid water with the use of test tube brush. The piston and barrel are then dried. The syringe is then reassembled and sterilized as for the new syringe. The sterilization of syringes in their glass containers and paper wrappers should be carried out in a hot air sterilizer for not less than one hour; if an autoclave is used the temperature of 120° is maintained for 20 minutes.



Fig. 1.

Method of suspending a syringe in a test tube prior to sterilization.

The needles.—After the syringe is used, the needle should be kept on the syringe while the cleaning process is carried out for the syringe. It is then removed from the syringe and the mount of the needle is cleaned out with a piece of cotton-wool on the end of a swab stick to remove any blood. The needle is then washed through again first with water and then with alcohol or methylated spirit and allowed to dry. Warming will accelerate drying. The point of the needle is touched up on a fine stone lubricated. A hand lens is used to see that the point is satisfactory. The needle is washed again thoroughly in spirit and dried. The silette is then passed through the needle to make sure that the bore is clear. The needle is then placed in a small glass tube inside a test tube (see figures 2 and 3), and the needles are sterilized in the hot air oven for one hour at 160° . The syringe and needle are removed from the tubes only immediately before use. Sterile forceps are used for the assembling of the syringe and the needle but the small tube covering the needle is only removed immediately before use. Some workers assemble syringes and needles and sterilize the whole thing in a glass container.

Less satisfactory is the disinfection of syringes by boiling. Syringes are thoroughly washed before they are boiled. The sterilizer should have a close fitting lid and a perforated tray inside. The piston and the barrel of the syringe and the needle and a pair of dissecting forceps are placed separately in water not above 50°C . in the sterilizer, the water is brought to boil and kept boiling for not less than 5 minutes with the lid on. The lid is then removed. The tray containing the syringe and needle is lifted out by means of a sterile forceps. The water in the sterilizer is poured away and the tray is at once returned to the sterilizer and the cover immediately replaced and left to cool. The syringe, the barrel, and piston are assembled with sterile forceps and the needle is fitted with sterile forceps and the assembled syringe is then returned to the empty sterilizer until it is needed. Wrapping of syringes, etc., in lint and sterilization by boiling is not recommended because it prevents their drying.

Disinfection of syringes by alcohol and chemicals.—This practice cannot be recommended. Chemical disinfectants have various disadvantages, they are unreliable and they may damage the material to be injected. The only chemical disinfectant that can be recommended is 70 to 75 per cent alcohol. Absolute

alcohol has very little disinfectant action. Attempts to disinfect a syringe by drawing and discharging spirit which is in common use is very ineffective. With all-

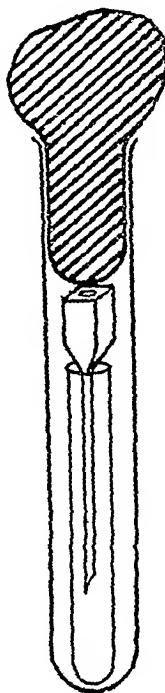


Fig. 2.

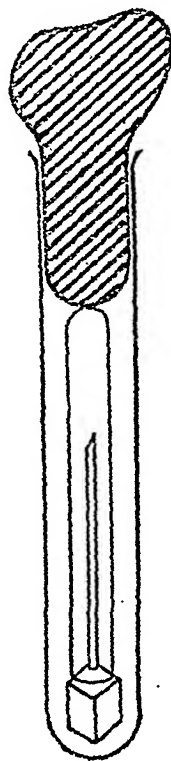


Fig. 3.

Alternative methods of inserting a needle into glass tubing, used as a guard, prior to sterilization.

glass syringes, immersion for 5 minutes in 70 to 75 per cent alcohol is fairly effective but glass-metal syringes cannot be disinfected satisfactorily in this way. The committee consider that alcohol disinfection should be used only when necessary and for no other purpose than the injection of sterile fluid. Syringes used for aspiration and for vein puncture should on no account be sterilized except by heat. Details are given regarding the extreme caution to be exercised in sterilizing all-glass syringes with alcohol. After disinfection by this method, the syringe must be placed in a sterile test tube or in a sterile container.

Disinfection by the hot oil method is discussed, but is not recommended. Needles however can be sterilized in hot oil if they are left for an adequate time and stored in the oil in which they had been heated.

The report then goes on to give details of the work of a team giving mass injections. They suggest a team of four, one doctor to give the injections, one assistant to look after and fill the syringes, another assistant to clean the skin of the patients before injection and a fourth to get the patient ready and keep the records. An adequate supply of syringes and needles is considered essential for this work. For inoculation purposes one syringe can be used for many injections—other than intravenous—but a fresh sterile needle must be used for each injection and the needles must be sterilized and kept covered until the very moment of use.

Mass intravenous inoculations are attended by special arrangements. A fresh sterile syringe and needle must be used for every patient. A large supply of syringes is essential

and facilities for rapid sterilization. For washing out syringes, a separate bottle of saline must be kept for each syringe. Sterile syringes should be handled with sterile forceps. The operator giving injections must not assemble syringes because his fingers may be soiled with blood from patients already injected. Similar precautions must be taken for all work involving the taking of blood samples for investigation.

A special section of the report deals with the care of needles, and regular inspection with a hand lens and sharpening of all needles not found in very good condition is recommended. Details of the bevels needed for different types of injections are given in the report.

Another section describes a syringe service for a hospital. A special department deals with the cleaning, sterilization and issue of all-glass syringes. The service involves the use of a large number of syringes but breakages are much reduced and complete sterility is maintained.

The final section of the report deals with certain special points such as the use of tuberculin syringes, and other syringes for special work. One syringe must be used for only one type of test. A trace of tuberculin remaining in the syringe may upset a subsequent Schick test. Moreover, different syringes should be used and reserved for different dilutions of tuberculin and for control injections. Similar remarks are made about Schick and Dick tests.

Syringes used for aspiration of infected material should never be used for giving injections. For aspiration a completely separate set of syringes should be used.

The appendices of the report deal with alcohol disinfection, pointing out how high concentrations of alcohol greatly reduce the efficacy

of disinfection; 75 per cent gives the best results. The possibility of spirit being contaminated is mentioned. The testing of syringes for leakage is described.

J. L.

THE COPPER SULPHATE SPECIFIC GRAVITY METHOD OF BLOOD ANALYSIS

IN a recent number (May, 1945) we reprinted the method of blood analysis by copper sulphate specific gravity bottles of Philips, van Slyke and others, and also wrote an editorial on it. The editor has been using this method with considerable success. He wishes, however, to draw the attention of the readers to one difficulty. Most of the copper sulphate available in India, both Indian and imported, contain impurities which make it unsuitable for use. If the bottles are made up with this copper sulphate, the specific gravity of the solution gradually falls and a precipitate appears at the bottom of the bottle, this precipitate consisting of oxidized impurities. The original article of Philips, van Slyke and others recommended copper sulphate United States Pharmacopœia standard, and some American (U.S.P.) copper sulphate is now being tried here. It appears, however, that the difficulty may be overcome only by using copper sulphate analytical reagent which at present seems to be unobtainable in this country. We have temporarily overcome the difficulty by recalibrating our solutions every few days by the use of accurate hydrometers, which are few and very difficult to obtain in this country.

J. L.

Medical News

COMPOSITION OF THE GRAIN OF WHEAT

(Abstracted from the *British Medical Journal*, 17th March, p. 379)

At a meeting of the Nutrition Society held at the London School of Hygiene and Tropical Medicine on 24th February, 1945, Dr. R. A. McCance and Miss E. M. Widdowson, discussing the superiority of wheat over all other cereals in its bread-making qualities, said that this property was closely linked with its protein content, which averaged 13.62 per cent in 'hard' Manitoba wheat with good baking qualities, but only 8.89 per cent in 'soft' English wheat, which was poor for baking. Laborious microdissections carried out at the Cereal Research Station of the Ministry of Food had shown that a typical wheat grain consisted of 12.3 per cent of bran, 83 per cent of inner endosperm, 2 per cent outer endosperm, 1.2 per cent embryo, and 1.5 per cent scutellum. The chemical composition and nutritive value of these fractions varied considerably. Thus the endosperm, from which white flour was derived, was rich in carbohydrate; bran was rich in iron; while the embryo and scutellum were rich in protein and fat. The distribu-

tion of vitamins also was uneven. Thus the scutellum, a tiny shield of powdery material interposed between the embryo and endosperm, contained more than half the vitamin B₁ of the whole grain. When low-extraction flours were milled the bran included the outer layer of the endosperm, known as the aleurone layer, as well as the germ and scutellum. A reduction in extraction from 100 per cent to 85 per cent involved only a small loss in vitamin B₁, but below 85 per cent the decline was rapid.

PRESERVATION OF CEREALS

Now that there is so much need for saving every seer of available food grains, it is surprising to learn that annual losses from rodents, insects and moisture amount to no less than three million tons. Such losses are deplorable, and if action can be taken to reduce them appreciably, a very great contribution to our food supply will have been achieved. With this object in view, Mr. F. P. Coyne of the Government of India Food Department has written a little handbook, *Principles of Cereal Storage* (Government of India Press, New Delhi) for guidance of storage officers. He

starts by considering the effects of climate on grain, moisture damage, then standard types of storage, grading of godowns and general hygiene which is the most important factor in good conservation. Insect pests of grain are then reviewed briefly. Fumigation is discussed in considerable detail and a short chapter on other control methods follows. The rodent problem is dealt with in the last two chapters; it is probably more serious than the damage from other causes. Given a good food supply, rats breed very rapidly, and even without breeding 100 rats will eat 27 maunds of grains in one year; besides they foul the grain, and a large amount is subsequently lost in handling and transport of torn bags. To prevent rat damage, the author recommends construction of rat-proof stores for which directions are given. The author's observations refer mainly to present conditions when large stocks are being held by provincial and state governments, but the principles, he says, apply equally well to holders of small stocks. Public health officers will find much of practical interest in the pamphlet.

THE INDIAN JOURNAL OF SURGERY VOL. VII, NO. 1, MARCH 1945

We have received a copy of the above number which contains the following interesting articles:—

Osteospondylosis condensans hereditaria by R. J. Weingarten and G. Politzer; teratoma of the testis by J. C. Paymaster; stricture of the common bile duct by O. V. Jhooma, malignant melanoma of the rectum by V. R. Mirajkar and Y. V. Sachdeva, and three articles followed by a discussion on carcinoma of the breast. A noteworthy feature of this number is two contributions from the American army, one on 'Some nutritional problems of surgical patients' by Colonel I. S. Radvin and the other on 'The place of the anaesthetist in the surgical team' by Lieut.-Colonel V. Goldman. Extracts and association notes are given at the end. The sixty-one pages of this number will be of much interest to surgeons in India.

LEPROSY IN INDIA VOL. XVII, NO. 2, APRIL 1945

This issue of this quarterly journal contains an interesting article on 'Trigeminal neuritis simulating leprosy' which is a condition of very rare occurrence. Dr. Cochrane's paper on 'Leprosy control with particular reference to Madras Presidency' published in the *Indian Medical Gazette*, is reprinted. There are also abstracts from current literature and four reports of a leprosy survey in Hyderabad (Deccan), and of three leprosy institutions.

SURGICAL LIGATURE CONTROL ORDER

An order of the Department of Education, Health and Lands, Government of India, dated the 23rd February, 1943, issued under the Defence of India Rules, lays down the conditions under which surgical ligature may be produced and marketed in this country. Ligatures can only be manufactured and sold under a licence issued by the Director-General, Indian Medical Service, who must satisfy himself that the applicant is in a position to fulfil the conditions. The manufacturer must provide and maintain an adequate staff, premises and plant for manufacture and testing, the testing being done under the supervision of the person approved by the licensing authority. Detailed records must be kept of each batch issued for sale; each batch is to be tested before it is put on the market. It must be sealed in a sterilized container of glass or other substance preventing the access of bacteria and must be marked in a manner laid down in the order. No person will be allowed to sell or distribute surgical ligatures or sutures unless it is labelled in accordance with the provisions of the order.

WINNING THE ANTI-MALARIA WAR ON BURMA FRONT

MALARIA, the greatest scourge of the East, is giving ground in South-East Asia before the unceasing attack by Allied forces. Control, unprecedented in the history of tropical medicine, has been achieved in the last few months.

Only two years ago 70 per cent of all army sickness cases in South-East Asia were caused by malaria. Last year the rate had fallen to 36 per cent and in the first four months of this it was down to 27 per cent. The figures now given show that the malaria rate has been reduced to 17 per cent of what it was at the corresponding time last year—0.32 per cent daily compared with 1.8. This swift progress has been brought about by the use of the suppressive drug mepacrine, by spraying with D.D.T. insecticide and by rigid anti-malaria discipline.

Measures on a scale and of a thoroughness never known before are now directed against the malaria-carrying mosquito. Both the army and the R.A.F. send out small research groups close behind our advancing troops to survey malarious tracts, to select camp sites and to plan ahead the tasks of malaria control units. Trickling jungle streams, seepage of swamps and clear water are canalized or attacked with D.D.T., for these are the breeding places of one of the most deadly malaria-carrying mosquitoes—*Anopheles minimus*—which caused most of the high malaria rate in Assam. Brackish swamps and lagoons lying near the sea are oiled or drained by deep channels into tidal streams. These are the breeding places of the *Anopheles sundaicus* mosquito, which infests the Arakan coast and has in the past won the notoriety for Cox Bazar, near the head of the Bay of Bengal, as one of the worst spots for malaria infection.

The D.D.T. insecticide was discovered by chance by a Swiss chemist about 75 years ago. The Germans were using it as an anti-lice agent. Successful experiments were made in Britain with this insecticide against malarious mosquitoes, and it was first used in the South-East Asia theatre last August. For a month after a room has been sprayed with D.D.T. it is a death chamber for the mosquito. It is sprayed in tents and buildings by low-flying aircraft over malarious tracts in the country.

The use of fish-net veils soaked in 'scat'—the American repellent—called dimethylphthalate gives the mosquitoes 'hot feet'. Dimethylphthalate is of the greatest value to forward troops who must sleep in slit trenches free from the encumbrance of a mosquito net. Close-fitting and wide-meshed veils and sleeves impregnated with the liquid keep mosquitoes away for 72 hours and used as a skin lotion the liquid is effective for two hours.

An important factor in the anti-malaria campaign is discipline in dress. To reduce the risk of mosquito bites, long trousers and buttoned sleeves must be worn particularly during the hours between dusk and dawn and mosquito nets must be used for sleeping.

All servicemen in this theatre east of the Brahmaputra must under military discipline take daily a tablet of mepacrine which prevents attacks of black-water fever, suppresses the symptoms of malaria and cures entirely the malignant tertian type of the disease. Though mepacrine discolours the skin as long as the men are taking their daily dose, it has no harmful effects.

Mepacrine was discovered by the Deutsche I.G. Farben-industrie in Germany. After the fall of Java when the Allies had to seek a substitute for quinine, intensive experimental work in Australia by Brigadier Hamilton Fairley proved that one-tenth of a gramme of mepacrine daily was enough to suppress the symptoms of malaria as long as the dosage was continued.

Yet mepacrine alone does not prevent infection. Though it cures the malignant form and suppresses the benign form, men can still be infected if sharp precautions are not taken. When mepacrine is discontinued, some of those bitten will suffer from the benign tertian malaria, the number and duration of

such cases depending on the number of times the men had been bitten.

UNIVERSITY OF MADRAS

THE Council of Post-Graduate Medical Education of the University of Madras, is arranging during January to March 1946, courses of lectures (not less than 20 in each) in Medicine, Surgery, Obstetrics and Gynaecology including recent advances in Pathology and Bacteriology, Ophthalmology and Oto-Rhino-Laryngology. The courses are intended for the benefit of medical practitioners preparing for higher degrees and diplomas and are open to any registered medical practitioner of the allopathic system of medicine. The fee for the full course is Rs. 100, or Rs. 50 for attending lectures in any one subject only.

The Council is also arranging, during the same period, Refresher Courses in Medicine, Surgery, Obstetrics and Gynaecology, for the benefit of the general medical practitioners. The course in each subject will be of two weeks' duration and will consist of bedside clinics, demonstrations of specimens, etc., and attendance at operations, wherever possible. The fee for the course will be Rs. 100 for the whole course or Rs. 50 for any one subject. The courses will be conducted in the Madras City Hospitals. Any practitioner who enrolls for the whole session on payment of Rs. 100 will be permitted to attend all the courses arranged by the Council.

Further particulars will be available from the Honorary Secretary of the Council by the 15th Novem-

ber, 1945, and candidates desirous of attending the course should register by the 1st December for the Refresher Course, and by the 25th December for the post-graduate course, by paying the prescribed fee, as the number of seats is limited.

W. McLEAN,
Registrar.

UNIVERSITY BUILDINGS,
CHEPAUK, MADRAS,
17th October, 1945.

BOMBAY MEDICAL UNION

THE Bombay Medical Union invites theses from members of the medical profession for the following two medals for 1945:—

- (1) Dr. B. S. Shroff Memorial Gold Medal. The following subject has been selected for competitive thesis: 'The significance of eosinophilia in tropical climates'. The thesis must be in six clear typed copies.
- (2) Dr. Sir Balchandra Krishna, Kt., Memorial Gold Medal. Preference will be given to any original or research work especially with reference to 'indigenous medicine on western lines'.

Each thesis should be designated by a motto instead of the writer's name and should be accompanied by a sealed cover containing the name and address of the writer and sent to the Honorary Secretaries, Blavatsky Lodge Building, French Bridge, Chowpatty, Bombay 7, by 31st December, 1945, for the first medal and by the 30th April, 1946, for the second medal.

Current Topics

Medicine in Jungle Warfare

By N. H. FAIRLEY, C.B.E., F.R.S.

(Abstracted from the *Proceedings of the Royal Society of Medicine*, Vol. XXXVIII, March 1945, p. 195)

DURING the earlier New Guinea campaigns casualties from sickness were five to thirty times as common as battle casualties, and malaria and dysentery proved a more serious menace than the Japanese.

Owing to the numerous diseases transmitted by biting insects the clothing of the soldier in the jungle is of major importance. Shorts are dangerous for though they are cool to wear, they increase the surface area of exposure to trauma and insect bites, increase the incidence of tropical ulcers, septic sores, dengue, filariasis and malaria and prevent the effective application of anti-mite fluid for the prevention of scrub typhus. Trousers, gaiters and long-sleeved shirts are essential in jungle warfare.

BACILLARY DYSENTERY

Dramatic evidence of the value of sulphaguanidine was obtained during fighting over the Owen Stanley Rangers on the Kokoda trail in 1942, when severe dysentery broke out in Australian troops. As the epidemic increased in severity, grave concern was felt regarding the dysentery casualties in the Australian forces. At this juncture all the available reserve of sulphaguanidine in Australia was rushed by air to Moresby and transported to the forward area, where all troops with diarrhoea were immediately treated. The result was remarkable. Within ten days the epidemic was completely controlled, and subsequently the incidence was reduced to the number of sporadic cases preceding the epidemic. It was the considered opinion of many officers in the A.A.M.C. that sulphaguanidine saved Moresby.

It is not proposed here to assess the relative merits of the different sulphonamides in the treatment of bacillary dysentery. Sulphaguanidine has to be given in large doses and is expensive. On the other hand, it has proved to be absolutely safe for Field use. In the thousands of cases of dysentery for which it has

been used in New Guinea, no instance of anuria has been reported, even though patients have been dehydrated in the initial stages of treatment, nor has agranulocytosis or exfoliative dermatitis been encountered. Rarely headache, nausea, mild erythematous or maculopapular rashes with or without slight fever has occurred, but toxic manifestations of any real severity have been absent. When it is remembered that the mortality in New Guinea from bacillary dysentery treated with sulphaguanidine is only 1:5,000, one has to be very sure not to add to it by substituting a more toxic drug. The disadvantages of sulphapyridine, sulphathiazole and sulphadiazine are their toxicity and especially their tendency to produce anuria in dehydrated patients.

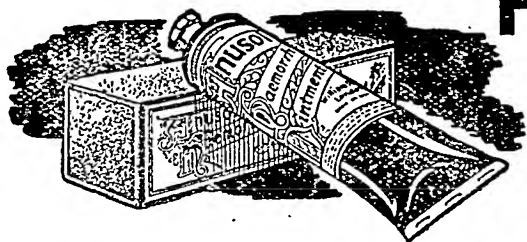
DENGUE

In the tropics and sub-tropics the rapid spread of dengue and the fact that it may prostrate as much as 60 per cent of a force make it formidable from a military view-point. Though the disease is non-fatal, it may incapacitate the victims for three weeks or longer.

Prevention.—No drug at present available will affect the course of this disease and no prophylactic vaccine is known. In New Guinea during an epidemic it was found that much could be done by: (1) eradicating breeding places in and around camps; (2) destroying adult mosquitoes by spraying tents and huts especially in the morning (8 to 9 a.m.) and later in the afternoon (4 to 7 p.m.); (3) wearing protective clothing and applying repellent lotion during the daytime; (4) keeping all febrile patients throughout the day and night under mosquito nets. Once a force has been exposed to an epidemic of dengue, sporadic cases may subsequently crop up from time to time, but they do not become numerous unless large numbers of non-immune reinforcements have been introduced in the interim.

MALARIA

So serious were the malaria casualties that in 1943 it was decided to create a research centre to investigate the precise value of all known anti-malarial drugs. The plan was to expose volunteers taking a specified



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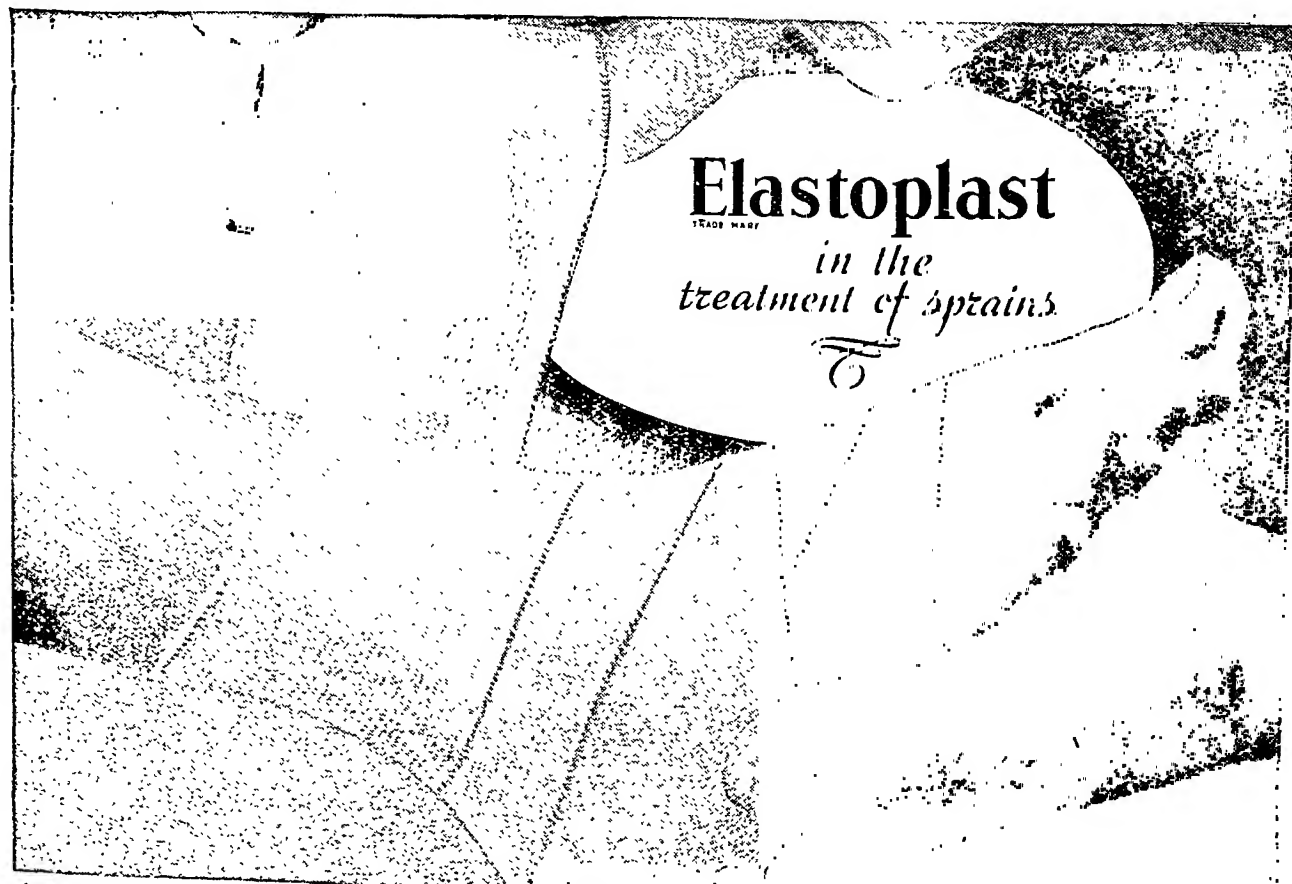
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daily dose of a given anti-malaria drug to bites of mosquitoes infected with *P. vivax* or *P. falciparum* parasites. Volunteers took the drug before, during and for twenty-three days after exposure to infection. The latter figure was selected as it constituted the upper limit for the ordinary incubation period for primary malignant tertian and benign tertian malaria.

Only brief reference can be made to the findings in volunteers infected with New Guinea strains of *P. vivax* and *P. falciparum* when taking quinine or atabrin (mepacrine).

Quinine.—*Malignant tertian malaria*: When volunteers, who were taking 10 grains of quinine daily, were exposed to ten infective bites by mosquitoes harbouring sporozoites of *P. falciparum* in their salivary glands, they invariably developed malignant tertian malaria with fever, splenomegaly and parasites in the blood within the usual incubation period. When the dosage of quinine was increased to 30 gr. daily the fever was rapidly controlled and generally parasites disappeared in three days.

Benign tertian malaria.—In volunteers exposed to ten bites of anophelines infected with *P. vivax*, 5 gr. of quinine daily were found inadequate to suppress over attacks of benign tertian malaria. When the dosage was increased to 10 gr. daily in another group of volunteers suppression was satisfactory in two-thirds of the cases.

Atabrin.—On the other hand, results quite beyond expectation were obtained in volunteers receiving one tablet (0.1 gramme) of atabrin for six or seven days of the week for four weeks prior to exposure to infection, during the period of exposure and for twenty-three days after the last infective bite. Controls not taking drugs who were bitten by the same number of infective mosquitoes from the same batch invariably developed malaria.

(1) *Benign tertian malaria*.—Volunteers exposed to bites of mosquitoes infected with *P. vivax* did not develop attacks of overt malaria when receiving atabrin with unvarying regularity in the above dosage. But in every case clinical malaria associated with parasites developed later, fever appearing in fourteen to forty-four days, and parasites from nineteen to forty-six days after drug administration ceased.

(2) *Malignant tertian malaria*.—Similarly volunteers exposed to ten to twenty-one infective bites (*P. falciparum*) failed to develop overt attacks of malaria when following an identical suppressive atabrin regime. Mild clinical features associated with a slight transient rise in temperature and perhaps some tenderness or enlargement of the liver and spleen were occasionally noted, but in no instance were symptoms sufficiently severe to necessitate bed rest and the volunteers invariably carried on their routine activities. In such cases parasites were never demonstrable though 1 to 2 c.mm. of the blood were examined in thick films. Furthermore, after cessation of drug treatment, overt malaria never developed. Sub-inoculation of fresh volunteers with 200 c.c. of their blood failed to produce infection, and susceptibility tests invariably showed the original volunteers were capable of developing malaria when they were infected with blood containing malignant tertian parasites.

(3) *Mixed infection*.—Reference has been already made to the fact that in jungle warfare most troops become infected with both *P. falciparum* and *P. vivax*. To reproduce field conditions experimentally it was therefore necessary repeatedly to infect troops by exposure to different batches of mosquitoes harbouring *P. vivax* or *P. falciparum* over a period of several months. In addition it was essential to subject them to conditions which favour malaria relapses such as physical fatigue, cold, anoxia, loss of blood, etc. All this was done, but in no instance did overt malaria develop while they were taking atabrin. But on an average of thirty days following cessation of drug administration every volunteer developed benign tertian malaria. Parasites of *P. falciparum*, however, were never found. These experiments were of profound significance from a military point of view for

they proved that, provided troops took atabrin in adequate daily dosage as laid down in standing routine orders, it was possible for them to go into hyper-endemic areas of malaria and fight for indefinite periods in the jungle without malaria casualties. Theoretically there would be no malaria admissions to hospital, no deaths, no carriers and no blackwater fever always provided the daily dose was continued for three to four weeks after leaving the endemic area. After stopping atabrin troops infected with latent *P. vivax* would develop overt benign tertian malaria.

Infective Hepatitis With Special Reference to Palestine

By E. LYON, M.D.

(Abstracted from the *Medical Press and Circular*, Vol. CCXIII, 14th March, 1945, p. 164)

COMPLICATIONS AND VARIATIONS

THE virus of infective hepatitis has a special tendency to settle in the liver so that in the majority of cases, apart from jaundice and slight elevation of temperature, other manifestations are rare. In a number of virus diseases other organ systems may also become involved, e.g. in the case of eruptive fevers the nervous system. Although the remarkable hepatrophy—similarly to the exanthema in those other diseases—acts as a protection for the nervous system, nervous involvement has yet—although very exceptionally—been reported (Markoff). One of my jaundice patients, a 37-year-old woman, also presented transitory meningeal irritation only recognizable by the raised lymphocytic count in the cerebro-spinal fluid (150 cells). In this patient jaundice persisted for 25 days, was accompanied by subfebrile temperature, while the liver remained swollen for five months. The patient, who had not had it before, was now suffering from constant headaches. In this case the virus had become lodged in the meninges. As Markoff points out, this is indicative of the virus character of the disease, which must be considered a general infection. It is paralleled by similar complications arising in the course of other virus diseases, e.g. measles, varicella, German measles, parotitis, infectious mononucleosis. They may all show the characteristic reaction in the cerebro-spinal fluid.

In a boy, aged 15, acute meningo-myelitis and radiculo-neuritis supervened on the ninth day after onset of jaundice and persisted for 10 days, starting with violent pain in the back and the small of the back, while later there was retention of urine, sensory disturbances and increasing weakness of the legs. No complete paralysis of the extremities, however, developed. Examination revealed flaccidity and abolishment of reflexes of the lower limbs. The patient made a complete recovery.

Markoff also reports virus-pneumonia as a complication of infective hepatitis. One of my patients developed an 'eosinophilic infiltration of the lung' prior to the onset of jaundice, and in another patient there was pneumonitis of the right lower lobe in the sixth week. In tropical and sub-tropical regions, basal pneumonia and amebic abscess of the right lower lobe, as well as infiltration of the lung in the course of icterus infectious Weil, should always be taken into consideration differential-diagnostics.

In a 19-year-old youngster whose heart had always been healthy, pulse liability persisted for four months after an attack of jaundice. Three electrocardiograms, taken at intervals of six weeks, were characterized by sinus-bradycardia with positive T-waves in all leads, rather tall and peaked in I, very tall and peaked in II and C. There were further supraventricular extrasystoles and right axis shift. The tall T-waves may be the consequence of a toxic factor (myocarditis?).

Although conjunctivitis is rather a common complication, iritis or papillitis are rare. Nose bleed was more frequent than skin hemorrhages (vitamin-K deficiency). Necrosis of the skin is rare and only

encountered in very severe cases (vitamin-A deficiency).

If the disease runs a protracted course, relapses may occur, so that after the jaundice has subsided and nearly disappeared it may flare up again.

Secondary to infective hepatitis we saw hypochromic anæmia, gastritis anacida, disturbances of the pancreatic function (neutral fats and muscle fibres in the stools). In one case, there was œdema of the head of the pancreas with stubborn jaundice. Chills as they are common in bacterial infection or malaria are absent in infective hepatitis.

With regard to the early and late complications and sequelæ of infective hepatitis, the clinical observations outlined above are in remarkable agreement with those made by Markoff.

THERAPY

The object of any therapeutic measure in infective hepatitis is to support the liver function rather than remove the infectious agent. Much harm is done by putting patients on too strict a diet. The diet should be high in carbohydrates with sufficient protein ($\frac{1}{2}$ to 1 gm. per kg. per day), with moderate addition of fat (20 gm. butter per day). Adequate protein intake is important, the optimum, being higher in the tropics and sub-tropics than in temperate climates. If the resistance of the liver is poor, particularly in elderly individuals or in pregnancy, adequate fixation of glycogen in the liver should be provided for at an early stage rather than wait until hepatic failure occurs. The patient should have 100-150 gm. of glucose per day, preferably diluted in lemon squash. Much benefit is also derived from intravenous injection of 30-50 per cent glucose solution, together with vitamin B, and C, since large amounts of carbohydrate in the diet require equally large quantities of vitamin B, and the carbohydrate-metabolism-regulating action of vitamin C also takes place in the liver, probably in a way that vitamin C facilitates the fixation of glycogen there. In the presence of nose and skin bleeding the patient should be given 10-20 mgm. of vitamin K, three times per day. Serious impairment of the hepatic function can, however, no longer be counterbalanced by vitamin K therapy. Although acute atrophy of the liver may be accompanied by lowering of the blood sugar, the indiscriminate use of glucose may cause much harm, since in the presence of serious hepatic lesion only very imperfect fixation of glycogen can be expected and hyperglycemia is likely to develop. Careful control of blood sugar is therefore imperative, and the administration of insulin together with adequate amounts of glucose indicated (5-10 units of insulin 30 minutes prior to glucose administration). Large quantities of insulin are likely to interfere with the carbohydrate metabolism in the liver. Hypoglycemia should by all means be avoided. Apart from arranging for an adequate caloric and vitamin intake, cellulose should also be given to maintain the intestinal function. Dietary prescriptions should therefore include: oatmeal soup, biscuits, rusks, vermicelli, rice, green vegetables (mashed), potato purée, grated carrots, lemon juice, tea, little milk; after a few days the patient may have two egg-yolks, some lean, boiled meat or fish. Alcohol should be strictly prohibited for a long time. As soon as the skin has resumed its normal appearance, the patient may be put on an ordinary diet.

The response to sulphanilamides is unsatisfactory. In five cases of infective hepatitis which in the initial stage received sulphonamides, in view of the influenzal character of the symptoms, the development into typical infective hepatitis could not be forestalled. The metabolism of higher micro-organisms is characteristically influenced by sulphonamides, while nothing is known about the way the metabolism of lower micro-organisms, including the virus of infective hepatitis, may react to the drug. The sulphonamide action consists in repression or destruction of a ferment system which viruses do not contain. If there were secondary coccal infection, this might be expected to

be amenable to sulphanilamide treatment. But this is not the case, and even an occasional success of sulphanilamide therapy does not establish the coccal nature of pneumonitis or pulmonary infiltration since they may also disappear without any treatment at all.

If the liver remains swollen and urobilinogen continues to be present in the urine, liver therapy may be indicated.

When reviewing therapeutic possibilities one should not omit the surgical aspect, particularly in cases in which the infection assumes alarming proportions. Intense jaundice may not be due to obstruction of bile ducts, as in the case of stones, but may be the result of events taking place in the liver itself, and the jaundice is then an 'intrahepatic' or 'hepato-cellular' one. After all internal measures are exhausted, surgical intervention, consisting in drainage of the bile ducts, may be our ultimate resort. Three of my patients in whom this necessity arose were operated upon, two in Europe who were cured and one in Palestine who succumbed. Cure has been reported after a drain had not even been introduced into the common duct but was only placed on the slit after division of the duct. Even just opening the abdomen or taking a biopsy specimen from the liver, although on this occasion the escape of large amounts of a sanguineous fluid was reported, was said to have had the same curative effect. Inflammation and œdema of the head of the pancreas may also be the reason for which jaundice may persist stubbornly. The proximal end of the common duct is normally imbedded in the head portion of the pancreas, so that inflammatory œdema of that part may very well cause obstruction. In one case a girl of 12, operation performed after jaundice had been present for nine months, revealed an indurated head of the pancreas and a union of gall-bladder and small intestine caused the jaundice to disappear immediately after operation. The child felt well, but 10 months after operation the spleen could still be felt enlarged and indurated.

Pulmonary Acariasis in Monkeys

By L. J. DAVIS

(Abstracted from the *British Medical Journal*, i, 7th April, 1945, p. 482)

IN view of the attention recently directed to the possible significance of mites in the causation of certain pulmonary disorders such as asthma, bronchitis, and 'eosinophil lung' in the tropics, it may be of interest to refer to earlier observations on pulmonary acariasis in monkeys, since this condition is probably known to but few medical men.

SOME OBSERVATIONS ON THE CONDITION

I first became aware of the phenomenon in 1933. When dissecting a *Macacus* monkey in Hong Kong I noticed small nodules scattered through the lungs. To the naked eye they resembled early tuberculous foci, although no other manifestations of tuberculosis were seen. On teasing out some of the nodules minute arthropods were found, which were subsequently identified by Dr. R. Hoeppli, of the Peiping Union Medical College, as mites probably belonging to the genus *Pneumonyssus*. The histological appearances are as follows:—

The nodules consist of capsules, the walls of which are composed of cellular granulation tissue. The lumen of each capsule is lined by epithelial cells and usually contains an arthropod lying among cellular detritus. The tissue comprising the walls of the capsules consists of fibroblasts, leucocytes, eosinophils, plasma cells, and endothelial cells. Very little formed fibrous tissue is seen and no giant cells have been noted. A constant feature is the presence of heavy pigmentation due to granules lying within histolytic endothelial cells. This pigment does not give a ferrocyanide reaction, and since it closely resembles similar

pigment visible within the gut of the parasites it is probably of faecal origin.

The eosinophils do not appear to be more numerous than is commonly seen in granulation tissue. Unfortunately, no hæmatological studies were done, so it is not known whether an eosinophilia was present in the peripheral blood.

The nodules are generally in close proximity to bronchioles, but in no instance could direct continuity be detected between a bronchiole and the lumen of a capsule. The surrounding lung tissue on the whole has a healthy appearance, although vascular congestion is excessive and erythrocytes are present within the alveoli in some areas.

Dr. Hoeppli drew my attention to a paper by Weidman giving a systematic description of similar acarids found in the lungs of a *Macacus rhesus* monkey in Philadelphia.

COMMENT

The demonstration in monkeys of pulmonary lesions due to mites might be held to lend strong support to the concept of pulmonary acariasis in man. If man be exposed to environmental conditions resulting in the aspiration of extraneous mites, it would be reasonable to suppose that, as in monkeys, structural lesions may ensue. That such lesions may give rise to symptoms requires no great stretch of imagination.

It would seem likely that the radiological findings, a remarkable mottled effect produced by small, discrete, ill-defined spots disseminated throughout both lung fields, resulted from lesions similar to those described in the monkey.

Pending the opportunity for post-mortem investigation of human cases, the experimental production of pulmonary acariasis in monkeys might be expected to throw further light on the problem.

Intramuscular Administration of Penicillin: A Method That Entails Only One Needle Insertion Daily

By R. S. LAHZ

(Abstracted from the *Medical Journal of Australia*, Vol. I, 7th April, 1945, p. 347)

At the Mater Misericordiae Public Hospitals, a simple technique has been evolved for intramuscular injection that obviates frequent reinsertions of the needle. The method has now been used for over six months, and no untoward sequelæ have followed its use.

The thigh is used as locus of injection—the antero-lateral surface in the lower half, the lateral surface on the upper half. The area selected is thoroughly

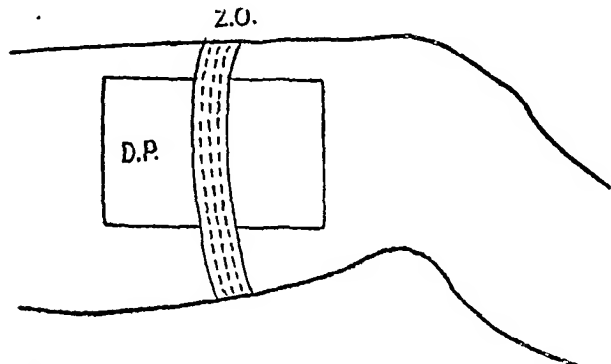


Fig. 1.—Z.O.=adhesive strip, D.P.=dressing pad. prepared surgically. A sterile dressing pad, six inches by three and a half inches in area, is laid over the point of injection, the latter being at the centre of the pad (figure 1). The pad is then fixed to the thigh by a strip of adhesive plaster long enough for the operator to be sure that the fixation is firm. The

pad is then doubled back over itself (figure 2) and thus covers the strapping on the pad. A sterile needle, whose size varies with the size of the thigh and the amount of fatty covering (in the average case three inches long and of bore 20), grasped by the hub only, is inserted obliquely in the muscles to within five-eighths of an inch of the hub which rests against the sterile pad. The penicillin is then slowly injected. On completion of the injection, before the syringe is detached, the needle is withdrawn five-eighths of an inch. The syringe is then detached. No penicillin

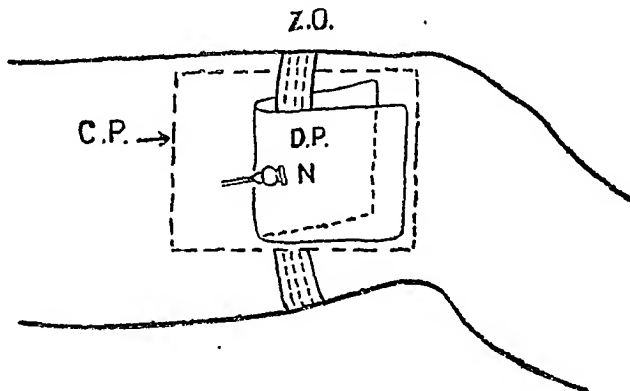


Fig. 2.—Z.O.=adhesive strip, D.P.=dressing pad, C.P.=covering pad, N=needle.

will run out. The needle and pad are then covered with a large pad wrung lightly out of some antiseptic solution. A crepe bandage is finally lightly applied.

When the next injection is to be given the covering pad is removed. The needle is reinserted five-eighths of an inch and the injection given. A fresh antiseptic pad covers the needle, after which it is again withdrawn five-eighths of an inch.

The fixed pad and needle are changed every twenty-four to thirty-six hours, when a new site is chosen.

We gave much thought to the antiseptic solution used in the covering pad, and have found satisfactory 'Monacrin' (1 : 1,000) or carbolic acid (1 : 21). Neither of these solutions causes irritation, even when used for ten days.

The operator should exercise scrupulous aseptic technique. Owing to the low temperature of the drug, the injection should be slow.

DDT in Action

(Abstracted from the *Lancet*, i, 10th March, 1945, p. 307)

It is now about five years since the insecticidal powers of DDT were discovered in the laboratories of Messrs. J. R. Geigy, A.G., of Basle. It proved to be lethal to lice and bed bugs at a tenth or less of the concentration required of the thiocyanates, which were among the most potent synthetic insecticides then known. This discovery came at a welcome moment for the Allies, who were experiencing difficulties in obtaining insecticides for controlling insect-borne diseases. Its chief virtues (apart from toxicity to insects) are chemical stability and physical inertia—in a word, its permanence. This contrasts with pyrethrum, which loses its insecticidal power rather easily in sunlight, especially when dispersed into small drops or thin films. On the other hand, DDT has one disadvantage in its slow speed of kill as compared with the rapid 'knock-down' of pyrethrum.

DDT is a white crystalline solid with a faint pleasant smell. It is practically insoluble in water but dissolves in various organic solvents fairly readily. The initials DDT stand for dichlorodiphenyltrichlorethane. Being nearly insoluble in water, DDT has very little smell or taste, so that one could eat large quantities without repugnance; therefore the question of toxicity

to man is important. DDT as an insecticide is quite safe. There is no recorded case of human intoxication by DDT despite the thousands of soldiers who have worn impregnated shirts and the considerable number of factory hands concerned with its manufacture and application, on the scale of several tons a day. The substance can penetrate the mammalian skin when in concentrated solution, but cannot do so when dry. Insects however can be fatally poisoned by mere contact with DDT crystals. The symptoms commonly shown by insects are twitching of the legs and lack of co-ordination; so they cannot walk or fly normally. These characteristic symptoms may persist for some hours before death. DDT has been found to be lethal to all types of insect on which it has been tested. But there may be wide differences in susceptibility. Simple tests in which half a dozen different insects were exposed to dry films of DDT on filter paper indicated a range of 10,000 : 1 in the doses necessary to kill.

For application, DDT can be made up as a powder, as a solution in kerosene or other liquids, or as a dispersion in water, or it can be dissolved in oil and the oil emulsified. The formulation is an important consideration in attacking different pests. For mosquitoes, DDT can be used either against the adult or the larva. For the adults, which are easily killed by it, DDT is a useful component of sprays and aerosols of various types. But perhaps the most promising method is to coat the walls of dwelling houses with a film of about 100 mg. per sq. foot which should remain lethal to mosquitoes for 2-3 months. This seems likely to be the most economical method of controlling malaria in native villages, and the consequence of its widespread use are enormous. In antimalarial oil DDT is toxic to mosquito larvæ at fantastically low rates. Under experimental conditions in West Africa, Buxton found that a tenth of an ounce per acre killed all larvæ (though it had no lasting effect). In practice, this dose has to be increased, to allow for poor distribution and to give some residual toxicity, to about 2-4 oz. Distribution of DDT dust by aeroplane is a novel and spectacular method but one which is of mainly war-time importance. Against houseflies and other muscids such as *Calliphora*, *Lucilla*, *Stomoxys*, and *Glossina*, DDT films are toxic for long periods, and this opens up new possibilities of their control.

For the control of body lice, DDT may be used either in the form of a dust (at 10 per cent in an inert mineral) or to impregnate underwear. The dust was used on a large scale in the Naples typhus epidemic early in 1944 and the successful control of the disease is generally attributed to the insecticide. The simplicity and speed of application by puffing dust under the clothes without troubling to undress people enabled very large numbers to be treated, which was a big factor in the success of the treatment. But this rough and ready method would only be effective with a highly insecticidal dust. A great advance in the protection of armies in the field from lice has been made in this war by the impregnation of underwear with insecticides. DDT is admirable for this purpose, only 1-2 per cent by weight of the garment being necessary. Owing to the insolubility of DDT in water, this 'proofing' resists a considerable amount of wear with weekly laundering.

For bugs, so far the most promising method seems to be the general spraying of walls and furniture with a 5 per cent solution in kerosene. The amount of DDT deposited should be at least 100 mg. per sq. ft. Field trials as well as laboratory work indicate that this deposit remains lethal to any bugs which may be introduced into a treated room for some three months.

Infection From Duck's Eggs

(Abstracted from the *Lancet*, i, 10th March, 1945, p. 314)

IN his annual report for 1926 the chief medical officer of the Ministry of Health drew attention to the

possibility that improperly cooked duck eggs could cause gastro-enteritis. This warning has been repeated many times, and W. M. Scott described several salmonella outbreaks in which duck eggs caused severe and often fatal infections. *Bacterium aertrycke*—or to give it its proper title, *Salmonella typhimurium*—has caused most of the trouble, but other salmonella types may act in a similar way. Gordon and Buxton have helped to close another link in the chain of evidence against the duck. They describe a case of gastro-enteritis in a man who had a fried duck egg breakfast and died six days later. *Bact. aertrycke* was found in his blood and faeces. Three of the four ducks which supplied his eggs gave serological evidence of *Bact. aertrycke* infection, but the results were variable. Of 16 eggs laid by the ducks, 3 contained the organism; it was isolated three times from both yolk and shell, from the ovaries of 2 of the ducks, and from the intestinal tract of the third. There is good evidence, therefore, that the fatal illness and the duck egg breakfast were related to each other; phage-typing of the duck and human strains of *Bact. aertrycke* might have clinched it.

Are ducks the only birds, domestic or wild, in this country which commonly transmit salmonella infections to man? The hen suffers from infections caused by a considerable number of salmonella types, and recent American work has shown that large epidemics of salmonella infections also occur among turkeys. Wood-pigeons, pheasants, and other birds are also occasionally affected. It is important to ascertain what part domestic fowls play in the spread of these infections and of the many new varieties of salmonella which lately appear to have come to stay with us. There is common ground here for the public health and veterinary pathologist, and it may well be that the domestic duck will soon have new company in the dock. Meanwhile there is something to be said for the German law which compels duck eggs to be indelibly stamped as such, and for the advice that they should be boiled for at least eight minutes or thoroughly baked.

Partial Starvation and Its Treatment

(Abstracted from the *Lancet*, i, 24th March, 1945, p. 375)

Discussing scarcity of food and effects of under-nourishment in parts of Europe, the article states:—

Straight starvation has been investigated in animals and man, as Magee reminded the Nutrition Society last year. Many have assumed that once hunger pains have disappeared, as they do about the fifth day, death from starvation is a gentle fading away, not entirely unpleasant: but unfortunately this may not be so. Magee pointed out that the body conserves the strength and weight of the nervous system, the skeleton, endocrines, and reproductive organs, and the losses fall on the skin, the muscles, and the digestive organs. The most noteworthy effects are on the alimentary system: the hydrochloric acid of the stomach decreases, the columnar cells are flattened, absorption is lessened, and intestinal ulcers develop, especially in the large intestine. These findings have been observed in man as well as animals and probably account for the diarrhoea simulating dysentery described in cases of severe malnutrition. It is perhaps worth noting that immunity reactions are lost by the starving, and it may be necessary to vaccinate them afresh if smallpox is about.

The nutritional oedema already mentioned in reports from the Continent is caused by having insufficient protein in a diet low in calories. The limited amounts of protein which would suffice if the calories were adequate are diverted to produce energy; the plasma thus becomes deficient in proteins, its osmotic pressure falls, and fluid leaks into the tissues and much salt in the diet is likely to increase this leakage. Children do not develop typical oedema, but are pale and doughy-looking. They become thin—that is, less

waterlogged—on being fed. When this œdema is combined with gastro-intestinal trouble the patient is in grave danger. Minor features, recalling nicotinic-acid deficiency and scurvy, are a red desquamated tongue and swollen inflamed gums. Major symptoms are dilatation of the stomach and a profuse watery diarrhoea, with frequent evacuations, often mistaken for dysentery. There are severe pains in the stomach and lower gut, and the diarrhoea leads to dehydration. Judging by recent reports nutritional œdema was seen among the French and Belgians more commonly during the first two years of occupation than it is now. After the early days these people supplemented their diet from an extensive black market, and so avoided the worst effects of the official ration. Neurological symptoms suggestive of vitamin deficiencies have not been generally described, though Simonart claims to have found neuritic signs which were relieved by injections of aneurin. Clinically his cases had more in common with nutritional œdema than with beri-beri.

The treatment of partial starvation was reviewed by Goodman in an address to the Medical Women's Federation a year ago. Mild cases will promptly respond to a diet of easily digested foods—particularly milk, eggs, meat, fresh ripe fruit, and cereals. (In view of transport difficulties, dried milk, even dried skimmed milk, dehydrated fish, and dried eggs will probably be used, and they should prove beneficial.) Much fat is contra-indicated, because of the diarrhoea. After a fortnight the patient should be able to take any ordinary diet, but absolute rest in bed for at least two weeks is highly desirable. Intermediate cases require hospital treatment and good nursing. Feeding should be cautious, beginning with milk and dairy products, and avoiding excess of fat. Pepsin and hydrochloric acid may be needed to help digestion, and mild diuretics to get rid of the œdema. Mercurial diuretics have been found dangerous: Evans and Perry thought that occasional deaths following the use of such drugs for cardiac or renal œdema might be connected with lowering of plasma protein; and this factor would of course operate also in the starving. Serious cases must have hospital care, good nursing, warmth and good food if they are to have any chance at all. They need frequent feeds of milk, gruels and lean meat, with pepsin and hydrochloric acid. Magee referred to the value of intravenous injections of glucose, and of opium to control diarrhoea. The prognosis is good in mild cases except when the patient is very old; in intermediate cases it is good for those between 20 and 40 years of age, but bad for the very young and very old; in serious cases it is bad for all ages, but those between 20 and 40 have the best chance. As so often, women have a better chance of recovery than men.

Of late years a new method of saving these severely ill patients has come into our hands: they can be nourished directly with protein digested into its component amino-acids, given intravenously with glucose. Severe inanition, nutritional œdema, and dehydration have responded to this measure, which was used during the famine in Bengal, and it has also given successful results with infants suffering from intractable diarrhoea, and with premature babies. Possibly the metabolic functions of the liver are helped by such hydrolysates. In Bengal the mortality among cases uncomplicated by pneumonia or malaria, treated in this way, is said to have been only 8 per cent, whereas control cases treated with glucose saline showed a mortality of 67 per cent. Cases of dysentery with intestinal ulceration are stated to have benefited considerably. Unfortunately, however, amino-acid preparations suitable for intravenous injection are still scarce. A single preparation ('Amigen') in America is said to be safe; other English and American preparations may produce febrile reactions. Nor can amigen be readily prepared in large amounts. Serum and plasma, though not as good nutritionally as protein hydrolysates, have some food value, and also reduce œdema by restoring plasma protein; and though they carry a risk of infective hepatitis, they may well be used to save life. The

important point is that the starving patient who cannot eat is no longer necessarily a lost man: we have found a new way of saving him, and must develop it.

Salmonella Infection

(Abstracted from the *British Medical Journal*, i, 31st March, 1945, p. 451)

THE micro-organisms classified as *Salmonella* strains comprise a bacteriological group allied to typhoid and dysentery bacilli but culturally and serologically distinct. Their wide distribution and the variety of diseases they cause in man and animals make them of great practical importance.

With widespread infections in domestic animals and animals having access to man, opportunities for transference to man are many, and *Salmonella* strains are of much importance as a cause of human disease. These infections fall clinically into three groups. One form is long-continued fever of the enteric type, often indistinguishable clinically from typhoid fever, and diagnosed only by serological and bacteriological methods: paratyphoid fever is the recognized example. A second type is that of severe acute gastro-intestinal irritation with rapid onset and comparatively short duration, which we recognize as a common variety of food-poisoning. It occurs in the form of outbreaks associated also with disease in animals, and this fact infected with a living *Salmonella* strain. In paratyphoid fever the incubation is long, but in this second type it is usually 12 to 24 hours. Until comparatively recently these were the only clinical varieties recognized, but over the past few years there have been many cases reported of infection with a *Salmonella* strain resulting in a septicæmia with a high mortality. Usually they appear as isolated cases, not in outbreaks, with no indication as to the source of the infection and without demonstrable relationship to other cases. The infection probably takes place through the intestine, but for unknown reasons blood infection occurs and general infection and localization in different organs. Thus the clinical manifestations are varied. S. Bornstein in a review of the salmonella problem, refers to clinical cases of endocarditis, meningitis, osteomyelitis, and other more rare conditions.

When the actual path of the infection from the salmonella source to the food is examined clear differences emerge. In paratyphoid fever the human carrier is either a chronic carrier, as is so common in enteric fever, or, more usually, a temporary carrier or an unrecognized ambulant case. It is useless to look for an animal carrier, because the paratyphoid bacillus does not infect animals. In food-poisoning of salmonella type it is of little value to look for a human carrier (apart from a case connected with a recent outbreak of food-poisoning), for persistent carriers of great rarity. On the other hand, the *Salmonella* strains which cause food-poisoning are all associated also with disease in animals, and this fact must be remembered when looking for the source of their introduction into food. The infection may be caused directly by eating the flesh of an animal suffering from a salmonella infection, through milk drawn from a cow so suffering, from infected duck's eggs, or most commonly from sound food infected indirectly, as from faeces of rats or mice. In the control of salmonella infections their wide distribution must therefore be borne in mind. The control of carriers and unrecognized cases is of essential importance in paratyphoid fever. An attack on animal diseases associated with salmonella infections is a long-term indirect method, but not a particularly promising one, of attacking food-poisoning. In all types of salmonella infection the care and preparation of food along the lines of strictest cleanliness are likely to yield the best results. In particular special attention is needed to prevent manipulated food from being kept before

consumption, at temperatures which allow multiplication of *Salmonella* organisms. Again and again it has been shown that a particular food—such, for example, as ham or a made-up dish—has been eaten fresh without harm, while the same food kept for a number of hours at a moderate temperature has become toxic and its consumption has set up a severe outbreak of food-poisoning. Outbreaks of food-poisoning are especially frequent during the hot months of the year.

Therapeutic Effectiveness of Penicillin in Treatment of Vincent's Stomatitis and Its Failure to Influence Favourably Certain Other Medical Conditions

By COLONEL J. S. SWEENEY

CAPTAIN W. J. MORGINSON

CAPTAIN R. W. ROBINSON

and

CAPTAIN E. M. KILPATRICK

(Abstracted from the *Journal of Laboratory and Clinical Medicine*, Vol. XXX, February 1945, p. 132)

Forty-three patients with Vincent's stomatitis were treated with from 6,000,000 to 1,000,000 units of penicillin. The antibiotic was given intramuscularly in doses of 25,000 units each three hours. The average total dose was 721,000 units. All of the patients were cured. After forty-eight hours of therapy, it was usually impossible to find fusiform bacilli and spirochaetes except in those in whom marked dental caries existed. In these patients, furthermore, the organisms disappeared rapidly after dental prophylaxis. It is interesting that oral temperatures frequently rose from a normal level to from 99.6 to above 101°F. during the time that penicillin was being administered. This phenomenon is unexplained and was not noted during the treatment of other diseases.

The paper also records the failure of this chemotherapeutic agent to influence favourably a number of other medical diseases, viz, asthma, malaria, rheumatic fever, lupus, chronic pyelonephritis, diphtheria, mumps, eczema, folliculitis, dermatitis herpetiformis, acute myeloid leucæmia, and follicular lymphoblastoma (Brill-Symmer's disease). One patient with a peritonsillar abscess failed to improve when given penicillin until the abscess was drained surgically. Several of the patients treated with penicillin also had trichophytosis; this latter lesion showed no improvement.

As for reactions, there was noted in only three patients a mild to moderate urticaria which disappeared within a few days during penicillin therapy.

The Male Climacteric

By A. A. WERNER

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXVII, 24th March, 1945, p. 705)

This report represents a study of 54 male patients each one of whom had one of the types of testicular hypofunction or a function. All patients complained of an intense subjective nervousness or a feeling of tension. This is especially noticeable on arising during the night or in the morning.

A large majority of these patients complain of sleeping poorly. They may be restless, sleeping only for short intervals during the night.

Numbness and tingling of the hands, feet or one or more of the extremities often occurs. Frequently these people awake while lying in bed and find the extremities completely numb.

Headache of various types and location occur that are rarely migrainous. They may be described as a dull to severe ache, usually not neuralgic, and may occur irregularly or be continuous. There are two types of headaches which have almost specific diagnostic importance in gonadal hypofunction: vertex and occipitocervical. The occipitocervical ache may radiate to the neck, over the scapular regions or down

the spine. The vertex ache is frequently described, as if a great weight were resting on the head, or as a feeling of pressure.

There is decreased memory and ability for mental concentration. Cerebration is slowed, and they are forgetful, especially for recent events.

Depression or mild melancholia is an important symptom; when this is present the patients have loss of interest in their work, in their home or in their past pleasurable diversions.

CIRCULATORY SYMPTOMS

Hot flushes are characterized by a sudden redness of the face and neck, upper chest and at times most of the body.

Tachycardia, palpitation and dyspnoea, more than usual on moderate effort, without evident cardiorenal disease is complained of. Walking a short distance, ascending a flight or stairs, almost any moderate effort causes cardiac consciousness.

Vertigo, especially with change of position, is often noticed, with no cardiovascular condition to account for it.

Cold hands and feet at any season are complained of by many of these patients.

GENERAL SYMPTOMS

Lassitude and fatigability are often present. Some of these people state that there is pronounced decrease of endurance, and they fatigue easily. Others complain that they are constantly tired or that on arising in the morning they are unrested or feel more tired than when they went to bed.

Constipation is frequently found in hypofunction of the thyroid and pituitary glands in which there is a relative vagotonia. Many of these patients complain of a gastric syndrome characterized by distention and eructation after meals with no organic lesions.

COMMENT

Testosterone propionate, by intramuscular injection of 25 mg. three times a week, has been found effective in relieving the symptoms and in the production of a sense of well-being in the patients, which is the primary objective of this treatment. This medication should be administered for two or three months. The patient may feel very well within a few weeks, but it is best to continue beyond this time for the purpose of stabilization. Testosterone may also be given orally, by inunction and by implantation. The effective oral dosage is three to eight times greater than by intramuscular injection. Inunction of testosterone is not so satisfactory. By implantation, one has no control of dosage.

Testosterone should not be given for the purpose of stimulating potency. While it occurs in some patients, this result cannot be promised and it is perhaps better for older men if this phase of the reaction does not result.

Sulphonamide Therapy in Gonorrhœa in the Male: Review of Four Years' Experience

By D. I. WILLIAMS

A. J. KING

and

C. S. NICOL

(From the *British Journal of Venereal Disease*, Vol. XX, September 1944, p. 97. As abstracted in *Bulletin of Hygiene*, Vol. XX, February 1945, p. 78)

THESE workers at the Royal Victoria Hospital, Netley, present a 'detached and considered assessment' of the problem of the chemotherapy of gonorrhœa, based on the treatment of some thousands of cases during the last four years. Most of the cases were treated with sulphapyridine, and schemes of dosage of varying intensity were used; 548 cases were treated

with 18 gm. of sulphathiazole in three days, a 76 per cent success rate being achieved with this one course of treatment, 21 per cent of these patients requiring adjuvant local treatment. Complications of the disease were rare and did not vary with the different schemes of dosage. Haematuria occurred in 15 out of 3,949 patients treated with sulphapyridine, but there were no cases of agranulocytosis. Nausea and vomiting were common after sulphapyridine but rare when sulphathiazole was used, and rashes and pyrexia hardly ever occurred (less than 0.5 per cent) when the period of administration was less than five days.

Analysis of the immediate results of treatment showed *inter alia* :—

(1) Sulphathiazole to be the drug of choice, chiefly on account of its relative non-toxicity. Over 100 cases were treated with sulphadiazine, with no better results.

(2) That a high initial dose appears to decrease the number of resistant (G.C.+) cases.

(3) That there is no reason ever to prolong treatment for more than four or five days.

(4) Sixty-six per cent of unsuccessful cases in which gonococci persisted failed to respond to further treatment with sulphathiazole, whereas 92 per cent of clinical failures not showing gonococci were so 'cured'.

The figures show a lower proportion of successes than those recorded by most observers, and the authors suggest that this may be due to the fact that they have included as failures not only 'gonococcus fast cases', but also those with persistent signs in all night urines which did not, however, show gonococci in urethral smears.

The Results of Adequate Control of Diabetes

(Abstracted from the *Medical Journal of Australia*, Vol. I, 28th April, 1945, p. 436)

THE close supervision of diabetes has not only extended their period of useful life, but has decreased the complications of the disease that otherwise might have threatened their comfort and safety. Russell Richardson and Morris A. Bowie have published a study on 100 patients who have had diabetes for ten years or more and who have been under constant care in one clinic for a period of at least ten years. For the past fifteen years these patients have taken a diet in which the fat content has never exceeded 110 grammes and has averaged 90 grammes; the carbohydrate has ranged from 125 to 200 grammes, and the protein, formerly reckoned at one gramme per kilogram of body weight, has lately averaged 70 grammes per day. One-quarter of the patients were men and three-quarters women.

Four groups of patients were distinguished; those in the first group took no insulin; in the second group the daily insulin intake was up to 25 units; in the third group 25 to 50 units; and in the fourth group 50 or more units were given daily. The degree of control of the disease was estimated by the range of the blood sugar level. The four groups here arbitrarily chosen include patients whose blood sugar levels are under 140 milligrammes, 140 to 180, 180 to 250 and over 250 milligrammes *per centum*. General observations showed that the disease did not always tend to become more severe. At the end of a five-year period in 45 of the patients no change was necessary in diet or increase in insulin requirements; in fact, in ten of them less insulin was required and in the remaining 55 increased insulin was accounted for in part at least by increases in diet. Chronic infections were relatively common and occurred in 39 patients out of the 100. Cholecystitis was the most frequently observed infective condition occurring in 16 cases.

The cardiac studies were interesting. Hypertension was present in 38 per cent of cases; all these patients were over fifty years of age. No connection could be traced between the duration, severity or degree of

control of the diabetes and the onset of hypertension. It is interesting to note that the incidence of cardiac enlargement in these patients was only about one-half that found in non-diabetic hypertensives. With this can be linked up the finding that the electrocardiographic changes often seen in hypertension with left ventricular strain were not observed in this series. Joseph Edeiken, who investigated this aspect of the inquiry, thinks that by comparison with records of other studies in the literature the value of the diet with the high carbohydrate and low fat content in reducing the incidence of cardiovascular complications is clearly indicated.

A further study of the peripheral circulation of these patients indicated that arteriosclerotic disease of the occlusive type was not common, and no serious incidents occurred. The ocular condition of the patients was also found to be satisfactory. Subcapsular cataracts were still found, but the incidence or degree of ocular sclerosis did not seem to depend on the degree of the diabetes. Deep retinal haemorrhages and exudates were found to increase with the duration of the diabetes and were only slightly decreased by closely observed treatment.

Too much emphasis must not be laid on the advantages of any one aspect of treatment, for there are many uncontrolled factors. For example, the excellent record of these patients in escaping serious vascular complications in the lower limbs is probably a tribute to the care bestowed on this feature of their treatment and the prompt correction of local infections by modern methods. But the record is a good one and should encourage those who patiently continue the supervision of the often refractory subjects of a life-time disease, in itself no easy task.

Another New Insecticide

(From the *Lancet*, i, 17th March, 1945, p. 347)

THE scarcity and high cost of pyrethrum and derris, whose active principles were until lately the most effective known insecticides harmless to mammals, have stimulated research into synthetic substitutes, and one of the compounds devised, DDT, has already proved a definite improvement on the vegetable products. Lecturing to the Society of Chemical Industry at Liverpool on 9th March, Mr. Roland Slade, *D.Sc.*, of Imperial Chemical Industries, Ltd., described another promising synthetic compound, the gamma isomer of benzene hexachloride, $C_6H_5Cl_6$, which has been named 'Gammexane'. Crude benzene hexachloride, first made by Michael Faraday in 1825, was found to be a useful though somewhat inconsistent insecticide, and ICI incorporated it in their flea-beetle powder in place of derris in 1943. Its activity, however, was soon observed to be almost entirely due to the 10 to 12 per cent of gamma isomer present. Gammexane is a colourless crystalline substance, melting at $112^\circ C.$, almost insoluble in water but soluble in organic solvents, practically inodorous, and with a bitter taste. It can be used as a spray in solution diluted with kerosene, or as a stable emulsion in water; it can be dusted as a diluted powder; or it can be volatilized on a hot plate, being stable at high temperatures. It has proved successful against wide range of insects and other pests, including house-flies, bed-bugs, lice, and fleas. When scattered at the rate of $\frac{1}{2}$ lb. per acre it killed 97 per cent of the larvae of *Aedes aegypti* in 2 days, and 100 per cent in 3 days; this compared with 43 per cent in 2 days and 97 per cent in 3 days with the same quantity of DDT. When tested against the African migratory locust, of which ICI maintain the only colony in this country, a bait containing 0.05 per cent of gammexane killed 96 per cent of the locusts in 2 days, whereas 0.2 per cent of DDT killed 57 per cent. A preliminary trial leads to the hope that gammexane will rid agricultural land of wireworms. Toxicity tests have shown it to be highly toxic to fish, but its toxicity to rats is low, 30 mg.

could be fed daily for 5 weeks without effect. These tests are no doubt being extended to other mammals, and as Dr. Slade said, its action on the skin will have to be carefully watched.

Detection of Nicotinic Acid Deficiency

(From the *British Medical Journal*, i, 21st April, 1945, p. 561)

LABORATORY estimations of vitamin B₁, riboflavin, and vitamin C in body fluids, such as blood and urine, have proved a tolerably good guide to the level of these vitamins in the human subject. This is not the case with nicotinic acid, which is not excreted entirely unchanged but is partly converted into derivatives such as nicotinamide, coenzymes I and II (di- and tri-phosphopyridine nucleotides), and nicotinamide methochloride or a related substance. It was formerly supposed that nicotinic acid was excreted partly as trigonelline, but this is now disputed by Coulson, Ellinger, and Holden, who believe that most of the so-called trigonelline is really nicotinamide methochloride. A few years ago attempts were made to diagnose nicotinic acid deficiency by estimating the urinary excretion of nicotinic acid or its derivatives, such as coenzymes I and II, in the blood. Experience has shown that such estimations are of little value for the laboratory diagnosis of disturbed nicotinic acid metabolism. Thus Spies and his co-workers noted a wide variation in the nicotinic acid content of urine both in the same individual and from person to person, even in pellagrins the nicotinic acid excretion is stated not to differ significantly from normal.

Najjar and his co-workers claim to have devised a specific chemical reaction whereby nicotinic acid deficiency can be quantitatively measured. By the adsorption of urine on zeolite and treatment of the eluate with alkali and butanol they have obtained a fluorescent pigment called 'F₂', which can be estimated fluorimetrically. The amount of F₂ excreted is stated to increase after the ingestion of nicotinic acid and several related compounds, and to be often absent from the urine of pellagrins. Further work by Huff and Pelweig suggested that F₂ was nicotinamide methochloride, but Ellinger and Coulson showed later that nicotinamide methochloride is not fluorescent in aqueous solution. F₂ is probably derived from nicotinamide methochloride by the action of alkali, and according to Ellinger and Coulson is a mixture of the *o*- and *n*-carbinol of N-methyl-dihydronicotinamide. Najjar, White and Scott have recently isolated F₂ in crystalline form from urine and studied its properties. According to them it is derived from N-methyl nicotinamide-carbinol and is probably the butyl ether of this compound.

In his latest paper Najjar proposes a test for the detection of nicotinic acid deficiency based on the measurement of N-methyl nicotinamide chloride in the urine instead of the fluorometric measurement of F₂. As N-methyl nicotinamide chloride can be conveniently prepared in the laboratory Najjar uses it as the standard of reference, the urinary output of N-methyl nicotinamide being expressed in terms of N-methyl nicotinamide chloride rather than in arbitrary fluorescent units of F₂, as done formerly. Najjar gives an oral test dose of 100 mg. of nicotinic acid, and estimates the urinary excretion of N-methyl nicotinamide during the following four hours. He considers an excretion of less than 2.1 grammes of the compound in this period to indicate nicotinic acid deficiency. Coulson, Ellinger, and Smart have also used the assay of nicotinamide methochloride in urine as an index of nicotinic acid nutrition in R.A.F. personnel. The nicotinamide methochloride of Coulson, Ellinger, and Smart appears to be identical with the N-methyl nicotinamide of Najjar. This method needs further investigation before it can be accepted. Thus, Ellinger and Coulson have shown that the excretion of N-methyl nicotinamide depends on a number of factors,

including not only the intake of nicotinic acid and its derivatives but also exercise, food, the presence of methyl donors in the tissues, and the deficiency of the methylating mechanism of the body. Sargent, Robinson, and Johnson consider that as a rule the level of F₂ in the urine runs parallel with the nicotinic acid intake, though they have observed well-nourished persons who excrete no F₂, and an excessively high excretion of F₂ during starvation. They also record that some subjects fail to show a larger excretion of F₂ after test doses of nicotinic acid. Mickelson studied two groups of young men on daily intakes of 10 mg. and 20 mg. of nicotinic acid respectively for nearly six months, and failed to observe any significant difference in the F₂ excretion in the two groups. Furthermore there was no difference in the F₂ excretion in the two groups after a test dose of nicotinic acid.

It is clear that we still have no simple laboratory method for estimating the level of nicotinic acid nutrition in man.

Intravenous Arsenic in Treatment of Anginous Forms of Glandular Fever

By K. S. SMITH

and

T. H. SHAW

(Abstracted from the *British Medical Journal*, i, 28th April, 1945, p. 581)

Six patients suffering from anginous glandular fever were treated with intravenous arsenicals. Speedy and conspicuous benefit was obtained.

The hæmatological findings in these and other cases are tabulated and discussed. In cases seen before the 12th day a conclusive diagnostic titre of agglutinations had already been reached.

The general treatment and management of very severe throat infections are considered.

Diagnosis is reviewed briefly from the standpoints of history, glandular enlargement, throat inflammation, hæmatology, and response to drugs.

Neutropenia was present at some stage in each of our cases. Its significance is discussed. Since sulphonamides are apt to cause neutropenia they are contra-indicated in this disease.

Oxaluria in British Troops in India

By J. M. BLACK

(Abstracted from the *British Medical Journal*, i, 28th April, 1945, p. 590)

THE most interesting feature emerging from a survey of urological cases admitted to the surgical division of a British General Hospital was the frequency of oxaluria as a cause of symptoms. Of the 77 cases investigated no fewer than 43 (55 per cent) were found to be suffering from oxaluria. Oxaluria was not diagnosed until a full investigation—viz, cytological and bacteriological examination of the urine, cystoscopy, and intravenous or retrograde pyelography—had been carried out.

Clinically oxaluria manifested itself in one of the three different ways shown in

Symptoms	Number of cases
Oxaluria with renal colic	20
Oxaluria with hæmaturia	15
Oxaluria with epididymitis and cystitis	8

DISCUSSION ON OXALURIA

It is well known that oxalate crystals can be passed in the urine for years without any tendency to calculus formation. Oxalates may be deposited at any reaction. Most commonly they are deposited after the urine has been passed and cooled. But they may be present

in vivo in suspension in the urine and cause irritation, and occasionally even slight hæmaturia. Microscopically they may be in the octohedral or envelope form, in the dumb-bell form, or in the biscuit form.

To avoid oxaluria, sorrel, rhubarb, and asparagus—which contain more than 2 g. of oxalic acid per kilogram—and excess of chocolate should be eliminated from the diet. The general opinion is that it is useless to try to control oxaluria by reducing the calcium intake or by increasing the magnesium-calcium ratio, and that neither acid nor alkaline therapy is indicated in cases of calcium oxaluria.

The frequency of oxaluria in the present series can be ascribed to (1) the climate—causing loss of body fluid by sweating and concentration of the urine; (2) the diet—inadequate fluid intake and the presence of oxalate-forming food in the diet (tomatoes, strong tea) Neville in 1935 found that oxaluria was apt to occur in vitamin-B deficiency, but in this series there was no clinical evidence of such deficiency. The association of amœbic dysentery with oxaluria noted by Manson-Bahr was observed in only two of our cases. The excessive formation of vitamin D by sunlight is said to be connected with tropical lithiasis.

All the stones recovered and examined consisted of a mixture of calcium oxalate and calcium phosphate. There was no pure oxalate stone. *Treatment* thus resolves itself into the prevention of oxaluria by: (1) Elimination of oxalate-forming foods from the diet. (2) Ensuring a fluid intake of adequate amount to prevent concentration of the urine. (3) In hospital cases, especially those requiring immobilization, a fluid intake of at least eight pints a day and ammonium chloride to prevent phosphatic deposit.

The Antidiuretic Action of Nicotine and of Smoking

By J. H. BURN
L. H. TRUELOVE

and

ISABEL BURN

(Abstracted from the *British Medical Journal*, i, 24th March, 1945, p. 403)

ALTHOUGH the effect of smoking in causing a rise of blood pressure has been known since 1907 (Hesse), that it does so cannot yet be said to be a matter of common knowledge. Recent observations by Roth, McDonald and Sheard provide fresh evidence on the point, and also demonstrate the fall of skin temperature due to the vasoconstriction of the skin which occurs. The rise of blood pressure, of pulse rate, and of vasoconstriction in the skin are all the result of the stimulation by nicotine of sympathetic ganglion cells. The observations recorded in this paper indicate that it is not only the nerve cells of the sympathetic ganglia which are stimulated by nicotine but that nuclei in the hypothalamus are also stimulated, as a result of which the hormone of the posterior lobe of the pituitary is liberated in the blood. The effect was accompanied in several of the observations by symptoms regarded as toxic effects of nicotine, such as vertigo, nausea, and even vomiting. These effects were not always present, and there is no doubt that the antidiuretic action is observed in their absence.

If smoking causes secretion of the antidiuretic hormone it seems reasonable to suppose that the other hormones of the posterior lobe, such as the oxytocic hormone, are also liberated. If this occurs, smoking should accelerate labour.

Many believe that there is a connection between smoking and gastric ulcer, and since Dodds *et al.* have shown that the injection of posterior lobe extract into rabbits causes gastric ulcer, it might appear that our experiments suggest the mechanism of the connection. This is very doubtful; large amounts of posterior lobe

extract are needed to produce ulcers, and the effect of pharmacopoeial doses of posterior lobe extract in man is to diminish gastric acidity, not to increase it. This we have observed here, in confirmation of other workers. Our experiments do, however, raise the question whether those with impaired kidney functions should be allowed to smoke.

SUMMARY

Nicotine exerts an antidiuretic effect in the rat. This effect does not occur if the pituitary body is removed.

Smoking exerts an antidiuretic effect in man. In a sensitive subject one cigarette will inhibit diuresis for 2 to 3 hours.

The same antidiuretic effect is produced in man by the injection of nicotine intravenously in an amount approximately equal to the amount absorbed from one cigarette.

It is probable that the nicotine absorbed from cigarette smoke stimulates the supra-optic nucleus of the hypothalamus and causes a discharge of the hormone from the posterior lobe of the pituitary gland.

Substances Used in Treatment of Pediculosis Capitis: Their Relative Value

By ELIZABETH B. S. SCOBIE

(Abstracted from the *British Medical Journal*, i, 24th March, 1945, p. 409)

A SERIES of laboratory and clinical tests is described in which an attempt is made to compare the efficiency of a number of 'cures' for pediculosis capitis. Some of the substances in common use are shown to be either ineffective or definitely inferior as insecticides and as ovicides. Any success obtained by their use can be ascribed largely to the mechanical removal of the lice by the careful toothcombing which is usually an important part of the treatment.

D.D.T. emulsion and lethane hair oil stand out as the two insecticides of value in the treatment of pediculosis. D.D.T. is preferable to lethane because one treatment properly carried out should cure every case. This substance will not, however, be available till after the war. Lethane will cure a large proportion of cases with one application, but two treatments at a week's interval will give certain cure. In order to obtain good results the details of the application of lethane should be carefully observed. Two or three teaspoonfuls of the oil are used for one treatment. The hair is parted, and 2 or 3 drops from the teaspoon or pipette are dripped on to the scalp. This is repeated in from 12 to 20 different areas all over the scalp. With the finger-tips the scalp is vigorously rubbed for two minutes to ensure equal distribution of the oil. Any oil which trickles down the forehead or behind the ears should be wiped off with cotton-wool and vaseline applied.

The following substances proved ineffective in the treatment of pediculosis: 20 per cent solution of dettol, derbac soap, concentrated infusion of quassia, 12.5 per cent formalin soap mixture, 0.1 per cent aqueous solution of mercuric chloride, oils of cedarwood, citronella, and lemon-grass and lauryl thiocyanate.

Nitrogen Loss After Thermal Burns Effects of Adding Protein and Methionine to Diet of Rats

By P. B. CROFT

and

R. A. PETERS

(Abstracted from the *Lancet*, i, 3rd March, 1945, p. 266)

1. METABOLIC experiments on burned rats show that increase in the dietary protein substantially reduces

the tissue wasting (with its accompanying loss of nitrogen in the urine) seen when the animal is maintained on diets of low or moderate protein value. This underlines the importance of high protein intake for patients suffering from burns, and suggests its value in other conditions where large areas of skin are lost.

2. The urinary losses in nitrogen after burning were reduced substantially by the inclusion of 1 per cent methionine in the diet. Neither alanine, nor a mixture of synthetic amino-acids, nor cysteine, had a similar effect. It is suggested that the apparent toxæmia is in reality a deficiency, induced by a call for one amino-acid with consequent raiding of a whole protein molecule.

3. During the period when patients suffering from burns cannot ingest much protein, methionine should be tried in the hope of stopping the nitrogen loss and consequent tissue wasting.

Penicillin-Albumin

(From the *Lancet*, i, 10th March, 1945, p. 314)

In their work on administration of penicillin by mouth, Harwood Little and Lumb found that if penicillin is dissolved in raw egg it will withstand changes of hydrogen-ion concentration which will seriously affect penicillin dissolved in plasma or milk and will destroy solutions in water, saline or cholesterol. In studying the efficiency of various penicillin mixtures given by mouth after a dose of alkali they concluded that a penicillin-egg mixture was the best; and, in their early experiments at least, it seemed that the blood serum remained bacteriostatic longer after such a dose than when penicillin is given intramuscularly. We now learn that, at the Squibb Institute in New Brunswick, Chow and McKee have shown that, unlike sulphonamides, penicillin, combined with human serum-albumin, retains its antibiotic activity. The penicillin-albumin mixture can be precipitated in 50 per cent alcohol and thus freed from unbound penicillin, which dissolves. The compound can then be redissolved in water and finally obtained in a dry powder. When given intramuscularly to mice it was more slowly excreted than sodium penicillin. Studies of its stability in acids and alkalis have not yet been published, but from the observations of Little and Lumb, we may hope that it will prove more resistant than ordinary penicillin to changes of pH such as it would encounter when given by mouth.

Bengal Famine

(Abstracted from *Science and Culture*, Vol. X, June 1945, p. 511)

A POST-MORTEM EXAMINATION has now been carried out on the Bengal famine of 1943. The Famine Enquiry Commission set up by the Central Government, with Sir John Woodhead (late of I.C.S.) as Chairman, has now released a report in which the situation prevailing before and during the famine has been analysed. The findings of the Commission are :—

I. That the incidence of the famine was not sudden, the signs of the catastrophe were apparent several months before its actual occurrence.

II. That although shortage of food supply and fall of Burma created conditions for its occurrence, its incidence was mainly due to (1) the sudden increase in the price of food materials, (2) the terribly low purchasing power of the people, (3) the confusion in the policy of the Government regarding control of prices and procurement of food grains through Government agents, (4) the panic in the adjoining areas after the fall of Burma, (5) the weak and vacillating policy of the Government to control hoarding and increase of prices, (6) the maldistribution of available supply, (7) unfortunate Government propaganda

against the incidence of famine when thousands were dying daily, (8) Government's failure to make an early declaration of famine and consequently delay in the adoption of relief measures, (9) unrestricted free trade, (10) export of rice from Bengal to other areas, (11) heavy purchases by the Army, huge stocks accumulated by industrial and Government employers, (12) destruction and loss of coastal boats, (13) lukewarm and complacent attitude of the Government of India and His Majesty's Government, (14) hoarding and greed for money even at the expense of human lives, and above all due to lack of enlisting public support and loss of public confidence in the capacity of the Bengal Government to take effective measures even under the most acute conditions.

The report says :

'A breakdown in distribution could be averted only by an intervention of Government, which would have the effect of restoring public confidence and of demonstrating to producers and traders the determination and the ability of Government to prevent a further rise in prices, and of assuring traders and consumers that the flow of supplies would be maintained.'

'The rise of prices was something more than the natural result of the shortage of supply which had occurred. It was the result of the belief of the producers, traders and consumers in Bengal at the end of 1942 and the beginning of 1943 that an ever-increasing rise in prices was inevitable and could not be prevented.'

'In the circumstances, an attempt to control prices by the prescription of statutory maxima aggravated the situation by driving stocks underground.'

'The failure of price control had caused a loss of confidence in the ability of Government to control the markets, and it was important that Government should demonstrate without delay their determination to prevent a further rise in price, and to assure traders and consumers that the flow of supplies would be maintained.'

'It has been reckoned that the amount of unusual profits made on the buying and selling of rice during 1943, was 150 crores. We cannot vouch for the accuracy of this figure, but beyond question huge profits were made. Popular views about large profiteers who speculated and hoarded amid growing distress, and the inability of Government to control them, were indeed not without foundation. There were such profiteers, but they were not the only culprits.'

'We have shown that by the end of 1942 all the signals were set at danger and that great efforts were needed to avoid catastrophe. We do not, however, wish to imply that famine, in the form in which it finally appeared, had become inevitable. The lack of political unity was a handicap, but the possibility of effective leadership of the people and effective action stimulated by such leadership had by no means disappeared. It may be that when this stage was reached, distress and starvation, in some degree, could not have been entirely averted. But opportunities for mitigating the famine and its lethal results still remained open.'

'We have been told that Government advised people that there was no shortage at a time when everybody knew that there was a shortage, and that this increased the prevailing lack of confidence.'

'Conditions actually prevailing in Bengal at the time were far too serious for anyone to believe anything of the kind. We consider that this propaganda of sufficiency was quite ill-advised. We think that it would have been wiser to have told the people the truth.'

'The remarkable feature of the Bengal famine was that the rise in the price of rice was one of the principal causes of the famine. This, as far as we are aware, makes it unique in the history of famine in India. The great majority of Indian famines have been caused by drought and widespread failure of crops over wide areas. Floods, hail, and cyclones have on rare occasions produced the same effect.'

'One of the reasons why the arrangements made by the Government of Bengal to deal with transport and other problems arising during the famine were unsatisfactory was that they failed to realize the magnitude of these problems and the scale of the organization required for their successful solution. Associated with this was a reluctance to appeal for outside help even when the organization and personnel available within the province were obviously inadequate. We feel that this attitude was particularly unfortunate in the circumstances.'

'The failure of the *aman* crop at the end of 1942, in combination with the whole existing set of circumstances, made it inevitable that, in the absence of control, the price of rice would rise to a level at which the poor would be unable to obtain their needs. It was necessary for the Bengal Government to undertake measures for controlling supplies and ensuring their distribution at prices at which the poor could afford to buy their requirements. It was also necessary for the Government of India to establish a system of planned movement of supplies from surplus to deficit provinces and States. . . . This rise in prices was the second basic cause of the famine. Famine, in the form in which it occurred, could have been prevented by resolute action at the right time to ensure the equitable distribution of available supplies. . . .'

'But after considering all the circumstances we avoid the conclusion that it lay in the power of the Government of Bengal, by bold, resolute and well-conceived measures at the right time to have largely prevented the tragedy of the famine as it actually took place. While other Governments in India were admittedly faced with a much less serious situation than the Government of Bengal, their generally successful handling of the food problem, and the spirit in which those problems were approached, and the extent to which public co-operation was secured stand in contrast to the failure in Bengal. . . .'

'Enormous profits were made out of the calamity, and in the circumstances, profits for some meant death for others. A large part of the community lived in plenty while others starved, and there was much indifference in face of suffering. Corruption was widespread throughout the province and in many classes of society.'

'It has been for us a sad task to inquire into the course and causes of the Bengal famine. We have been haunted by a deep sense of tragedy. A million and a half of the poor of Bengal fell victim to circumstances for which they themselves were not responsible. Society, together with its organs, failed to protect its weaker members. Indeed there was a moral and social breakdown, as well as an administrative breakdown.'

Reviews

BOOKS RECEIVED

1. Midwifery: Principles and practice for pupil midwives, teacher midwives and obstetric dressers. By R. Christie Browne and Barton Gilbert. With 'Infants' Section'. By R. H. Dobbs. Second edition. 1945. Published by Edward Arnold and Company, London. Pp. xii plus 831. Illustrated. Price, 15s.
2. Essentials of local anaesthesia in dentistry. By A. C. Bowden. 1945. Published by John Wright and Sons, Limited, Bristol. Pp. 60. Illustrated.
3. The elements of medical treatment. By Sir Robert Hutchison. Fourth edition. 1945. Published by John Wright and Sons, Limited, Bristol. Pp. 213.
4. Medicine in Britain. By Hugh Clegg. Published for the British Council by Longmans, Green and Company, London. Pp. 47 with 10 photographs. Available from Longmans, Green and Company, Limited, 17, Chittaranjan Avenue, Calcutta. India.
5. Local anaesthesia brachial plexus. By R. R. Macintosh and William W. Mushin. Published by Blackwell Scientific Publications Limited, Oxford. Pp. 56. Illustrated. Price, 10s. 6d.
6. Hey Groves' Synopsis of Surgery. Edited by C. P. G. Wakeley. Twelfth edition. 1945. Published by John Wright and Sons, Limited, Bristol. Pp. viii plus 632. Illustrated. Price, 25s.
7. A textbook of psychiatry for students and practitioners. By D. K. Henderson and R. D. Gillespie. Sixth edition. 1944. Published by Oxford University Press, London, Humphrey Milford. Pp. xii plus 719. Obtainable from Oxford University Press, Bombay and Calcutta.
8. Recent advances in neurology and neuropsychiatry. By W. Russell Brain and E. B. Strauss. Fifth edition. 1945. J. and A. Churchill Limited, London. Pp. xiv plus 363, with 32 illustrations. Price, 18s.
9. The premature baby. By V. Mary Crosse. 1945. Published by J. and A. Churchill Limited, London. Pp. viii plus 156, with 14 illustrations. Price, 10s. 6d.
10. Cleft palate and speech. By M. E. Morley. 1945. Published by E. and S. Livingstone Limited,

Edinburgh. Pp. xii plus 160. Illustrated. Price, 7s. 6d. Postage, 4d.

11. Massage and medical gymnastics. By M. V. Lace. Third edition. 1945. Published by J. and A. Churchill Limited, London. Pp. xi plus 244, with 128 illustrations. Price, 12s. 6d.

12. A textbook of surgical pathology. By C. F. W. Illingworth and B. M. Dick. Fifth edition. 1945. Published by J. and A. Churchill Limited, London. Pp. viii plus 728, with 306 illustrations. Price, 42s.

13. Diseases of the nervous system. Described for practitioners and students. By F. M. R. Walshe. Fourth edition. 1945. E. and S. Livingstone Limited, Edinburgh. Pp. xvi plus 360. Illustrated. Price, 15s. Postage, 7d.

14. Textbook of medicine. By various authors. Edited by J. J. Conybeare. Seventh edition. 1945. Published by E. and S. Livingstone Limited, Edinburgh. Pp. xx plus 1164. Illustrated. Price, 30s. Postage, 9d. (Home).

15. Acute injuries of the head: their diagnosis, treatment, complications and sequels. By G. F. Rowbotham. 1945. Published by E. and S. Livingstone Limited, Edinburgh. Pp. xvi plus 424, with 201 illustrations, 12 in full colour. Price, 30s. Postage, 7d. (Home).

16. Revel without a cause: The hypnoanalysis of a criminal psychopath. By Robert M. Lindner. 1945. Published by Research Books Limited, London. Pp. xi plus 259. Price, 21s. Available from Messrs. William Heinemann (Medical Books) Limited, 99, Great Russell Street, London, W.C.1.

17. Fractures and orthopaedic surgery for nurses and masseuses. By A. Naylor. 1945. Published by E. and S. Livingstone Limited, Edinburgh. Pp. xii plus 288, with 243 illustrations. Price, 16s. Postage, 7d. (Home).

18. Vaccination therapy. By K. M. Hiranandani. Published by Dr. K. M. Hiranandani. Near Rasala Road, Hyderabad, Sind.

19. The essentials of chiropody. By Charles A. Pratt. 1945. Published by H. K. Lewis and Company, Limited, London. Pp. xii plus 156, with 34 illustrations. Price, 10s.

Service Notes

APPOINTMENTS AND TRANSFERS

COLONEL J. W. VANREENEN, O.B.E., V.H.S., is appointed Honorary Physician to The King, with effect from the 17th July, 1945, *vice* Colonel R. V. Martin, C.I.E., Indian Medical Service, retired.

Lieutenant-Colonel W. Scott, Civil Surgeon, Amraoti, is transferred as Civil Surgeon and Superintendent, Robertson Medical School, Nagpur, with effect from 10th July, 1945.

Captain Mehar Chand Sharma, I.A.M.C., Deputy Controller in the Office of the Drugs Controller, India, Bombay, has been appointed as Assistant Controller-General of Civil Supplies, with effect from the forenoon of the 1st July, 1945.

The undermentioned officer reverts from R.I.N.V.R. and is seconded to the Indian Army Medical Corps:—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Captain P. S. Clarke. Dated 17th May, 1945.

The undermentioned officer is transferred to the General Service Cadre, with effect from the date specified:—

Captain K. N. Raman. Dated 1st June, 1945.

To be Captains

Gurdev Singh. Dated 5th February, 1944.

Kalipada Ganguly. Dated 14th April, 1945.

To be Lieutenants

Jadab Chandra Karmakar. Dated 15th April, 1945.
Melville George Allen Mersh. Dated 24th April, 1945.

Gerald Justin Kenneth Peck. Dated 1st May, 1945.

19th May, 1945

Pardip Kumar Basu Roy. Dilip Kumar Sen.

Bhagwat Prasad. Dated 20th May, 1945.

The undermentioned officer of the I.M.S. (E.C.) reverts from I.A.M.C. and is seconded for service in the Indian Air Force:—

Lieutenant D. K. Roy Choudhury. Dated 14th November, 1943.

INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

(WOMEN'S BRANCH)

To be Captain

Mylai Ranganatham Jannabai. Dated 16th April, 1945.

To be Lieutenant

Elizabeth K. Markos. Dated 14th April, 1945.

The undermentioned officer of the Indian Medical Service reverts from R.I.N. and is seconded to the Indian Army Medical Corps:—

Surgeon Commander W. Mackie. Dated 15th June, 1945.

PROMOTIONS

Major to be Lieutenant-Colonel

B. S. Nat. Dated 20th November, 1944.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

Captains to be Majors

G. H. F. Humphreys. Dated 3rd April, 1945.

L. B. Belkhole. Dated 1st May, 1945.

S. C. Roy. Dated 17th May, 1945.

D. F. Mehta. Dated 20th May, 1945.

2nd June, 1945

N. K. Roy. B. B. Chatterjee.

G. A. Flann. Dated 3rd June, 1945.

R. K. Chettur. Dated 6th June, 1945.

B. H. Syed. Dated 17th June, 1945.

T. A. Mirza. Dated 19th June, 1945.

K. J. L. Scott. Dated 20th June, 1945.

22nd June, 1945

S. R. Chatterji. S. S. Chatterjee.

R. J. Henderson. Dated 24th June, 1945.

C. W. A. Searle. Dated 26th June, 1945.

S. D. I. Herekar. Dated 27th June, 1945.

M. A. Mannan. Dated 28th June, 1945.

L. M. Kelly. Dated 29th June, 1945.

Lieutenants to be Captains

3rd June, 1945

H. P. Vaishnava. M. Anis-ur-Rahman Khan.

A. Jayachandran. Dated 6th June, 1945.

P. V. Ramanarao. Dated 14th June, 1945.

M. A. Mughni. Dated 16th June, 1945.

M. Azhar-ul-Haque Siddiqi. Dated 17th June, 1945.

S. N. H. Abidi. Dated 17th June, 1945.

B. C. Banerji. Dated 18th June, 1945.

INDIAN MEDICAL SERVICE—SECONDED TO THE INDIAN
ARMY MEDICAL CORPS

(Emergency Commission)

(WOMEN'S BRANCH)

Lieutenant to be Captain

(Miss) D. W. Smith. Dated 23rd April, 1945.

RETIREMENTS

Lieutenant-Colonel B. H. Singh, M.C. Dated 14th December, 1944.

Lieutenant-Colonel J. H. Barrett on account of ill health. Dated 28th December, 1944.

RESIGNATION

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

Captain B. N. Singh. Dated 14th May, 1945.

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The Editors of *The Indian Medical Gazette* cannot advise correspondents with regard to prescriptions, diagnosis, etc., nor can they recommend individual practitioners by name, as any such action would constitute a breach of professional etiquette.

In India, Dr. C. G. Pandit of the King Institute of Preventive Medicine, Guindy, reports (personal communication) the diagnosis of five

cases of the disease in Bellary Jail in 1922 by the workers of this institute, and says that sporadic cases continue to be encountered by them. In East India many sporadic cases of *B. paratyphosum C* infection have been detected

(thanks to the Army Medical Services) mostly among civilian labourers hailing from Bengal, Madras and Nepal. Out of 16 cases seen in the writer's experience 9 are briefly described in the following table :—

Age and history	Course of disease	Laboratory findings	Results
1. Age 15.	Rapid onset with fever and chill. Lungs clear; spleen and liver not palpable; tongue furred; bowels costive; pulse rapid and full. Remittent fever 9 days, patient delirious, toxæmic and apathetic, suggestive of typhus. Fifteen days after onset, generalized tenderness and agonizing pain in the musculature particularly in the thighs. No arthritis, abscess formation or leucocytosis (see figure 1).	Blood negative for malaria parasites. Blood culture positive for <i>B. paratyphosum C</i> on 7th day. Weil-Felix and Widal (To, Ao) repeatedly negative. Total white cell count 9,050. Stool and urine cultures negative. Direct serum agglutination with <i>B. paratyphosum C</i> 1 : 830, 51 days after onset.	Recovered.
2. Age 25. History of fever 6 days.	Constipation. Temperature remittent throughout; pulse rapid. Cough and expectoration; on 10th day lungs showing signs of broncho-pneumonia. Restlessness and delirium, marked prostration and apathy, congested eyes, suggestive of typhus (see figure 2).	Blood negative for malaria parasites. Weil-Felix negative. Blood culture sterile. Post mortem—Lungs congested, œdematous; a few subpleural petechial hæmorrhages. Liver enlarged, fatty, very friable. Bile thin, golden yellow; bile culture showed <i>B. paratyphosum C</i> . Spleen $\times 2$, soft and not defluent. Mesenteric glands enlarged.	No response to sulphapyridine and antimalarial drugs. Patient died on 15th day.
3. Age 20. History of fever 4 days.	Remittent temperature for 10 days; patient toxæmic and apathetic. From 11th day temperature intermittent. Both ankle joints swollen, tender and painful on 12th day; arthritis (see figure 3).	White cell count 10,400. Blood cultures sterile. Widal (To, Ao, Br. abortus) and Weil-Felix repeatedly negative. Stool and urine cultures negative. Direct agglutination of serum with the organism 1 : 7,500 and later 1 : 3,750.	Complete recovery after 15th day.
4. Age 23. History of 5 days' fever with cough.	Spleen palpable. Developed severe pain in chest and extensive râles; broncho-pneumonia, giddiness, vomiting, toxic look, coated tongue and dehydration. Temperature remittent, then intermittent and at the end subnormal (see figure 4).	Blood culture <i>B. paratyphosum C</i> on 11th day. B.T. rings in blood smear. Stool and urine cultures repeatedly negative. Total white cell count 26,400. Post mortem—Pneumonic patches in lower lobes of both lungs. Liver enlarged and fatty; spleen soft and dark-pink on section. Two oval hæmorrhagic patches in intestines 5 inches and 8 inches; colonic mucosa congested. Small multiple abscesses on surface of kidneys.	No response to sulphathiazole or antimalarial drugs. Died on 25th day.
5. Age 35. History of 4 days' fever with diarrhœa. Anæmic.	Spleen palpable. Low temperature for 8 days. Feeble pulse, apathetic. Scattered crepitations at right base of lungs (? typhus). Intermittent temperature 4 days (see figure 5).	X-ray of lungs normal; white cell count 20,050. Blood culture <i>B. paratyphosum C</i> . Widal (To, Ao) negative. Weil-Felix—OX19 rose from 1 : 386 to 1 : 770; OXK insignificant. Stool and urine cultures repeatedly negative. R.B.C. 2,880,000.	Completely recovered after 12 days.
6. Age 35. History of fever and rigor 3 days. Repeated attacks of malaria.	Liver and spleen enlarged 1 finger, tender. Remittent temperature throughout. Pain in right hypochondrium. Crepitations over left lobes of lungs. Persistent hiccough and marked abdominal distension not relieved by enemata. On 7th day, apathetic, poor cerebation, drowsy, twitching of face. Blood pressure 115/70. Retention of urine (see figure 6).	Post mortem—Lungs congested, no consolidation. Spleen enlarged; smear showed M.T. schizonts. Liver markedly enlarged, cloudy swelling, friable, lobule degeneration, subcapsular hæmorrhages; bile culture showed <i>B. paratyphosum C</i> . Mesenteric glands enlarged. Kidneys, cloudy swelling and general pallor.	Died on the 8th day.

Age and history	Course of disease	Laboratory findings	Results
7. Age 25	Irregular temperature, not affected by antimalarial treatment. Duration 6 days (see figure 7).	Blood smear showed B.T. rings. <i>B. paratyphosum C</i> isolated from stool culture. Widal (T_0 , A_0) and Weil-Felix negative. Direct agglutination with <i>B. paratyphosum C</i> 1 : 125 on 21st and 1 : 50 on 25th day.	Mild case. Recovery.
8. History of fever, headache and vague pains 2 days.	Spleen 3 fingers, liver 1 finger, tender. Friction rub over right axillary region, and a few crepitations over right lower lobe of lung, no consolidation. Remittent fever 8 days 100°F. to 104°F. followed by intermittent fever 3 days (see figure 8).	Total white cell count 8,400, polymorphs 85 per cent, lymphocytes 15 per cent. Blood culture— <i>B. paratyphosum C</i> . Widal (T_0 , A_0) and Weil-Felix negative.	Mild case. Uneventful recovery.
9. History of fever 3 days, and shortness of breath and asthmatic attacks.	Lungs—extensive rhonchi, expiration prolonged. Liver just palpable and tender. Remittent temperature for 6 days and low intermittent fever 3 days (see figure 9).	White cell count 6,800 and 12,000. Blood smear negative for malaria parasites. Blood culture— <i>B. paratyphosum C</i> . Widal (T_0 , A_0) and Weil-Felix negative.	Do. 7

Note.—The isolated organisms were invariably confirmed by Central Military Laboratory, Poona. The confirmation of the last two cases is awaited.

Clinical features.—Some cases are mild, others extremely grave and even fatal. The onset is sudden. Grave cases may be associated with severe toxæmia and apathy, often simulating typhus fever. No rash has been met with, though Garrow (1920) reports on a proved case (European) from East Africa with rose

in some cases, especially with pulmonary complications, which range from bronchitis to frank pneumonia. Tenderness and enlargement of the liver is not uncommon. Constipation rather than diarrhoea is the rule. There is no jaundice, and there may be multiple abscesses and arthritis.

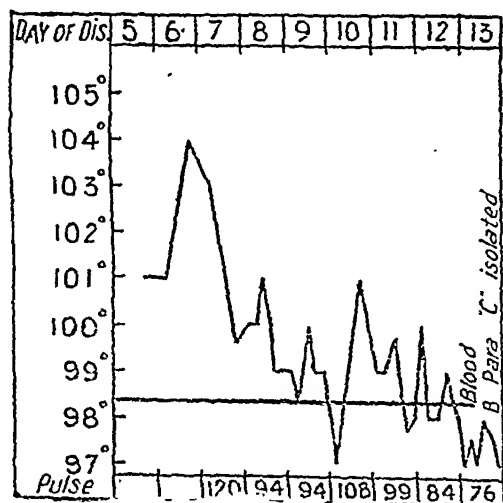


Fig. 5.—Mild case—recovery.

spots on the abdomen. A remittent temperature followed by an intermittent temperature is the general pattern of temperature charts (see figures). The period of remittent temperature is the period of anxiety, while the intermittent phase is associated with improvement in general condition. The pulse rate is proportional to the rise of fever, and leucocytosis is met with

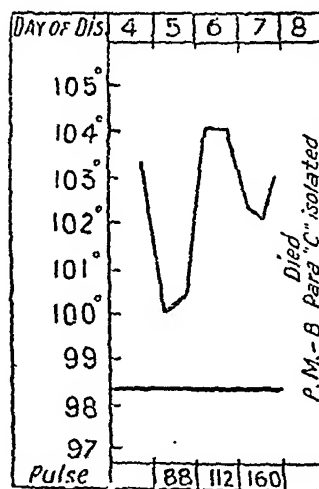


Fig. 6.—Fatal case with concurrent malarial infection.

Pathology.—The disease appears to be primarily a septicæmia with localization of infection in the biliary tract, etc. (Todorovitch, 1925). Post-mortem reports, including those described by other workers, show the following general features:

The intestines show no abnormality apart from congestion or even hæmorrhagic areas in the

small intestine and colon; solitary lymphoid follicles and Peyer's patches are not affected, nor is ulceration met with. The mesenteric glands are generally enlarged. The liver is generally enlarged with extensive fatty changes; the architecture of the lobules may be destroyed; subcapsular hæmorrhages or even necrotic areas

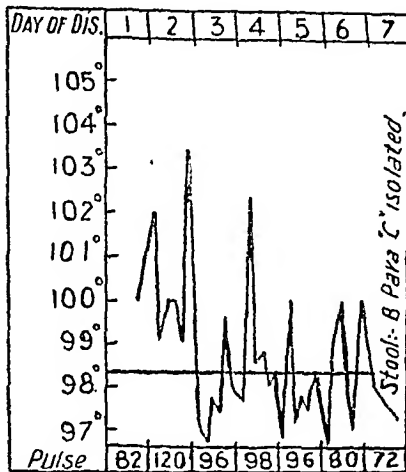


Fig. 7.—Mild case with concurrent malarial infection.

may be met with; the bile is thin, golden-yellow in colour; liver smear or post-mortem bile culture shows *B. paratyphosum C*. The spleen may be slightly enlarged and soft, but not diffuent; dark pink on section. The kidneys invariably show cloudy swelling and fatty change giving a general toxæmic appearance; the normal

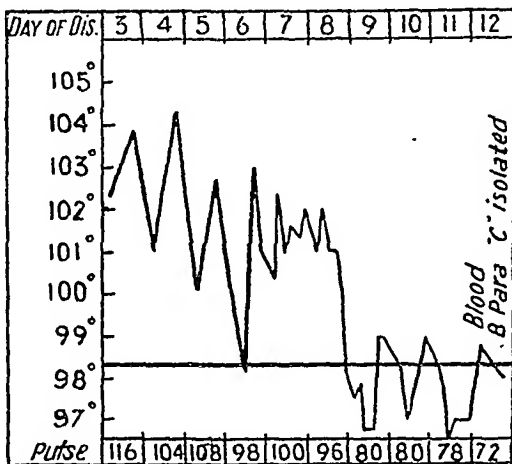


Fig. 8.—Mild case.

cortical structure may be destroyed; the capsule strips easily; the stellar veins may be prominent and there may be pin-point hæmorrhages or even pustules over the surface of the organs. The lungs may show congestion, subpleural hæmorrhages and lobar or broncho-pneumonic signs when organisms may be isolated from lung smear. The heart may show subendocardial and subpericardial hæmorrhages. The brain shows

nothing abnormal. There may be suppurative arthritis, gluteal and multiple cutaneous abscesses.

Diagnosis.—The diagnosis primarily depends upon the isolation of the organism from blood culture. In one case the diagnosis was made by isolating the organism from the stool, and from

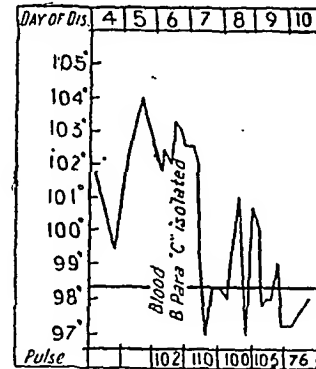


Fig. 9.—Mild case with concurrent asthma.

the consideration of the clinical state. A raised agglutination titre against the suspension of this organism is strong evidence of the infection. Cultures of sputum in cases with pulmonary complications, of purulent material, e.g. septic joints, gluteal and cutaneous abscesses, and of post-mortem pathological material such as bile, etc., also help in the diagnosis. Only the first three methods were employed for the diagnosis of cases recorded here; post-mortem bile culture in all cases of unexplained pyrexia has been the routine procedure in our hospital.

Treatment.—This has been entirely on symptomatic lines, with plenty of fluids and wholesome diet, and sulphapyridine in cases with pneumonic signs.

Discussion

Patients with atypical patterns of fever have been encountered in this country, but the diagnosis is missed either due to infrequent and late blood cultures or to the absence of *B. paratyphosum C* suspensions in routine Widal tests. Incidentally, the Director, Pasteur Institute, Shillong, reports that not a single case of *B. paratyphosum C* infection has been so far met with after hundreds of blood cultures and agglutination tests done by them. A similar reply was received from the Director, Epidemiological Bureau, Government of the Punjab.

Andrewes and Neave (1921) while describing a case in England compared *B. paratyphosum C* with other members of the salmonella group in detail. Hirschfeld prepared his quadruple vaccine (containing T.A.B.C.) for routine inoculations in Serbian troops. Similar vaccines were tried in the Belgian Congo and in the British Army in the Near East in the last war. Dudgeon and Urquhart (1920), while working in Anglo-Serbian hospitals, examined serologically the

blood of 20 volunteers 10 days after the inoculations and found an active response to T.A.B. antigens, but a C reaction occurred in only one case in whom it was already present before the inoculation. A similar absence of C reaction was found in the case of Serbian soldiers believed to have been inoculated with Hirschfeld's vaccine, whereas similar experiments with the rabbit's serum elicited a uniform response to each member of the quadruple vaccine. They found that agglutination reactions after inoculations appeared to have no relationship with the number of bacilli injected; they were not only uncertain, but may be entirely absent.

Summary

Nine cases of paratyphoid C fever are described.

The available literature on the subject is reviewed.

The importance of the addition of *B. paratyphosum* C suspension in routine Widal test is stressed.

Acknowledgment

Thanks are due to Colonel W. MacAdam, I.A.M.C., Officer Commanding I.G.H. (IT), for permission to report the cases, to the Director, Pasteur Institute, Shillong, for permission to study the available literature in their library, and to Major J. C. S. Paterson, R.A.M.C., Officer Commanding Field Laboratory for various investigations.

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INTRACRANIAL HERNIATION SYNDROMES

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An increase in the intracranial tension, brought about by a neoplastic growth, a vascular catastrophe, an inflammatory condition,

or an occlusion of the normal channels of circulation of the cerebrospinal fluid, naturally manifests itself in various forms. The controlling factors seem to be the pressure-dynamics of the cerebrospinal fluid and the brain tissue and, to a less extent, of the supporting bony lines, the cranial cavity in adult being rigid and inelastic.

It is well recognized that the symptom-complex may consist of general signs of intracranial hypertension, e.g. headache, papilloedema, vomiting, bradycardia and mental torpidity, or on the other hand it may express itself by signs of a gradually progressive local lesion alone, if the underlying process is a destructive one. It is however not well recognized that changes in the tension in the two intracranial chambers, namely the supra-tentorial and the sub-tentorial, may bring about the displacements of the brain tissue *en masse* or in parts. It is intended in this paper to emphasize the importance of such displacements of cerebral and cerebellar tissue.

Increase in intracranial pressure may be generalized, affecting both the supra- and infra-tentorial compartments, or it may be confined to either compartment and even to the right or the left half of one compartment. A deviation of the falx cerebri from its medial position, or a depression or raising of the tentorial diaphragm may be caused. As Rowbotham states: 'During some phase in the rise of supra-tentorial pressure, a process of brain tissue from the under and inner surface of the temporal lobe (uncus) herniates through the opening of the tentorium. The midbrain is displaced and compressed against the opposite free edge of the tentorium. The compression may be unilateral but is frequently bilateral between two herniated processes. Conduction of impulses from the cerebrum is impaired, and the neural mechanisms below the compression are released from the control of the higher centres.'

'A similar herniation of the lower poles of the cerebellum may occur into the foramen magnum along with caudal shift of the medulla, produced by a depression of the tentorium produced by a uniform increase in supra-tentorial pressure. Here the compression occurs about the level of the pons and the medulla. In the case of cerebral herniation, a primitive postural state known as decerebrate rigidity develops, which is well known from animal experiments, and follows transection of the brain stem just below the red nucleus. The muscles of the limbs go into a state of extreme hypertonus usually in a position of extension but occasionally in flexion. If, on the other hand, the Deiter's nucleus or its descending axons in the vestibulospinal tract are compressed, the decerebrate rigidity is replaced by spinal flaccidity.'

Below are given reports of two cases, one of decerebrate rigidity and the other of decerebrate flaccidity. In the former, a spontaneous

subcortical hæmorrhage caused herniation of the uncus into the tentorial hiatus. The decerebrate flaccidity was caused by pressure of the cerebellar herniation on the upper part of the pons brought about by an internal hydrocephalus. An exact interpretation of signs in both cases could not be made, because of an absolute lack of localizing signs; in the first case, although a raised intracranial tension was apparent, flaccidity of the musculature could not be explained till the post mortem revealed the cerebellar 'corking'.

(1) *A case of spontaneous subcortical hæmorrhage with decerebrate rigidity*

A sweeper, aged 20 years, admitted on 24th April, 1943, for the treatment of pain in the right side of the neck and chest of eight days' duration, and inability to swallow both fluids and solids, due to a feeling of obstruction in the gullet.

The patient stated that he had carried a bundle of clothes about 10 days before; 2 days later he felt the pain in the neck, about the middle of the right sternomastoid muscle. The pain gradually increased in intensity and extended to the greater part of the neck, right shoulder and chest.

There was no history of dog bite or any open wound before the onset of the complaint. The patient had not taken any food other than the ration food of the hospital.

Examination revealed a rigid spasm of all the muscles of the neck and body. The jaw muscles, masseters and temporals were firmly contracted, though the mouth could be opened almost completely. The neck muscles were very tense on both sides but he could move the neck from side to side, though flexion was difficult and painful. Respiration was shallow, the chest and abdominal muscles being tense, with the pectorals, latissimi, and recti abdominis all standing out in contraction. There was no obvious spasm of the muscles of the upper and lower extremities.

The patient was in obvious distress and pain, but lying quietly and in one position, and sweating profusely. Attempts at examination caused further spasms of the pectorals and the abdominal muscles, but no opisthotonus.

The tongue was easily protruded; no apparent spasm; moist and clean. Pharynx soft, palate moves freely, no congestion of membrane. Eyes—all movements unimpaired; pupils equal and reacting to light and convergence; no congestion or coloration in conjunctivæ. Heart not enlarged; no murmurs; rate slightly accelerated. Pulse of normal volume and tension. Lungs equally resonant on both sides; breath sounds vesicular and without accompaniments. Abdomen—a board-like rigidity of muscles; liver and spleen not palpable; abdominal reflexes not elicited; tendon jerks—all slightly brisk; plantar reflex—flexor.

No sensory changes except that any painful stimulus caused a spasm of all muscles of the body.

Progress and treatment

24th April, 1943. 10 a.m. Lumbar puncture was attempted without success. On placing the patient in a lateral position, he assumed an opisthotonic position, with head well extended, suggesting a basal meningitis. Treatment with sulphapyridine and intravenous glucose saline was instituted.

The rate of flow of intravenous fluid, in spite of the clamp not being used, was very slow, indicating spasm of the deeper musculature of the body. Later that day there was increasing spasm of the lower extremities in extension, and that of the right limb was noticed to be more marked than the left. Calcium lactate injections were given with no improvement.

That evening there was profuse sweating, marked over the face and neck.

The veins of the neck were now becoming prominent, but no visible pulsation was seen. The heart rate rose from 84 to 120 per minute. The pulse still bounding.

At 8 p.m. the patient complained of difficulty in passing urine. The bladder was found distended, and 28 oz. of urine extracted by catheterization.

Next day, the patient was apparently in the same condition, still virtually as stiff as a log. On turning on to his side, he moved *en masse*, sweating profusely. There was a rise of temperature in the afternoon T/P 102°/120.

Lumbar puncture was done under morphia, and 20 c.cm. of cerebrospinal fluid were removed. No increase in tension, and no microscopic or chemical abnormality was found. The patient was passing urine normally, but as he was not able to eat any food, it was decided to give a large dose of paraldehyde per rectum to secure some relaxation.

In the evening the patient suddenly had hiccup, the spasm of the diaphragm being very apparent in the sudden bulge of the abdomen, with retraction of lower costal area and the epiglottic sound. This was immediately followed by the regurgitation of about 2 oz. of 'coffee-ground' fluid from the stomach.

The patient began having tonic spasms in which his back arched backwards, the elbows were pressed against the side, the knees extending completely and the feet going into the equino-varus position, the teeth tightly clenched and facial muscles also in spasm. But there was no spasm of the hands and forearms, though the elbows were every time flexed. During these spasms a good deal of saliva collected in the mouth and was later spat out forcibly. Antitetanic serum, 160,000 units intravenously and 40,000 units intramuscularly were given.

The spasms persisted right through the night, though under the effect of morphia the patient had fairly good sleep. There was no relaxation of the muscles.

On the third day he spat out about 4 teaspoonfuls of blood-stained purulent material, the source of which could not be detected. Under the microscope the material proved to be pure blood and mucus.

T/P 100°/84. No improvement in general condition.

That night, on completion of a glucose saline infusion, the patient went into a very severe spasm involving the glottis, and for the first time the hands. The face became blue and cyanosed, the neck veins standing out prominently, eyes bulging, with corneæ gradually becoming lustreless, and the cardiac impulse becoming more and more diffuse. Just when death seemed imminent, the spasm relaxed and gradually an increasing amount of air entered the chest. There were, however, repeated complete but short spasms every 15-20 seconds for the next 5 minutes. Slight spasms persisted, causing great distress to patient.

The next day, the eye specialist reported—pupils normal; muscles moved normally; media clear; fundi normal.

Anæsthetics were given intravenously in the evening which produced an almost complete relaxation of all muscles and the patient had a fairly restful night, but as its effect began passing away the spasms returned again.

The next day the patient was drowsy, but the general condition further deteriorated. T/P 102°/120. Pulse low in volume and tension. Spasm of muscles persistent. Speech and circulation began to be affected; pain in the area of the glottis. The general condition deteriorated further next day, the pulse became rapid and weak and the patient died in the night.

Post-mortem report.—(Only abnormal findings.)

1. Bilateral hæmatomas in rectus abdominis muscles. A well-localized subcortical hæmorrhage, sausage-shaped in the left frontal lobe, running antero-posteriorly. A small leakage point present, from which hæmorrhage extended into the subpial space over an area about 2 inches square in the fronto-parietal region. Slight herniation of the inferior and medial surface of the both temporal lobes into the tentorial hiatus.

Commentary

The features of this case strongly suggested tetanus, and throughout the duration of the disease, this malady remained uppermost in one's mind; but clinically the case did not look like one of tetanus.

The short incubation period, the absence of an open wound at any time, and the ability to open the jaw almost completely throughout, were against such a diagnosis. When the patient spat out semi-purulent blood-stained material, it was thought that a deep-seated abscess harbouring the tetanus bacillus might have burst into the pharynx, but microscopic examination disallowed such supposition. The administration of antitetanic serum brought about no improvement in the patient.

Clinically, tetany was excluded by the fact that rigidity was generalized and persistent, and did not consist of cramps of any particular group of muscles. Even after a prolonged spasm enough to produce an acidosis, there was no relaxation of the muscles. The classical signs, namely Chvostek's and Trousseau's, were not elicited and there was no response to intravenous administration of calcium with or without parathyroid.

The fact that there was no history of dog-bite and the patient had already survived for eight days, entirely ruled out the possibility of hydrophobia.

Strychnine poisoning too was excluded for obvious reasons.

A unilateral subcortical hæmorrhage (as revealed by post mortem) later bursting through and spreading on the surface of the brain can explain the bilateral clinical picture only by the supposition that the rise of intracranial tension in the upper chamber of the skull, brought about by the hæmorrhage, led to the development of a tentorial pressure cone causing decerebrate rigidity.

It is surprising that pressure on the third nerve which usually is a complication of tentorial pressure did not occur in this case.

(2) A case of internal hydrocephalus

A driver, aged 30 years, was admitted on 17th February, 1945, with the following complaints: (i) diarrhoea and vomiting of 24 hours' duration, (ii) headache and backache of one month's duration. The disease started with a feeling of giddiness, a rigor and pain in the abdomen; he had vomited twice and passed four motions.

The patient was slightly collapsed; hands and feet were cold to touch; rectal temperature 98.6°F., pulse 76 with diminished tension. He showed improvement with intravenous saline and sulphaguanidine.

Thirteen days later, the patient got up during the night to defæcate, felt giddy and fell down; he complained of severe pain in the back of the neck, and felt weak. There was no stiffness of the neck and no physical signs. A week later he had an attack of hiccup for about 10

hours and so was sent up for neurological examination.

History.—The patient stated that for about 4½ months he had been experiencing attacks of weakness of the left lower limb which usually accompanied a headache of bitemporal type. Both these lasted 2 to 3 hours and occurred 4 to 5 times a day. Each time the weakness occurred, the patient experienced difficulty in using his leg to press the clutch of his car. A fortnight later there was weakness of the left arm as well, which gradually extended to the right limbs. Two months ago while on guard duty he felt pain in the back of the neck, which has persisted; for the past fortnight he has been noticing numbness and tingling in both extremities.

The patient was fully conscious and intelligent; there was pigmentation on the dorsum of the hands; no rigidity of neck; but venous pulsation in external jugular veins present. The heart was slightly dilated, sounds feeble, and rate 48. The function of the cranial nerves was normal except for a sharp nystagmus to the left and slow to the right.

Sensory system.—Pain and touch sensations impaired in patches over the lower extremity but fine touch sensation was intact, as also were all the deep senses, e.g. joint sense, deep pressure, movement, etc.; slight tenderness of the calves.

Motor system.—Paresis of all the four limbs, more in the left limbs and most in the left lower limb, accompanied by a very marked flaccidity in proportion to the weakness, apparently of the lower motor neurone type but without wasting or fibrillation.

There was slight inco-ordination of the left upper limb in the finger to nose test.

Reflexes.—Pupils equal, regular, reacting to light, convergence. Abdominal reflexes lost in all quadrants. Plantar reflexes flexor on both sides. Tendon jerks slightly more brisk on the right than on the left, both in upper and lower extremities. Ankle clonus present on both sides, more sustained on the left.

Gait staggering with a slight tendency to fall to the left. Fundus normal.

Lumbar puncture showed fluid under low pressure; only 2 c.cm. were obtained.

Five days later the analgesia spread all over the body except in the central facial region; the left upper limb was almost completely paralysed; there was paresis of all limbs with marked hypotonicity of the muscles. The patient was unable even to sit up, but peculiarly there was no wasting of any muscles. The plantar reflexes were still flexor; there was some stiffness of the neck, and for the first time some rigidity was felt at the elbow towards the end of passive extension on the left.

A week later the patient complained of intense, throbbing, bitemporal headache and loss of sleep but was inclined to be drowsy. Paralysis and atonicity increased in all regions;

With the hope that it may be beneficial as well as diagnostic, a cisternal puncture was done; there was no drainage of fluid spontaneously or by suction. Soon after, the patient showed signs of rapidly developing central respiratory failure, became gradually cyanosed and unconscious, and died.

Post mortem.—The meninges appeared normal. On lifting the brain off the base of the skull, the posterior perforated space was greatly enlarged and the cerebrospinal fluid flowed out of it like a fountain. The inferior pole of the left cerebellum, and a very small part of that of the right, were herniated into the foramen magnum. The roof of the 4th ventricle was adherent to the inferior surface of the herniated cerebellum, and the foramina of Luschka and Magendie could not be defined. All the four ventricles, the foramen of Munro and the aqueduct of Sylvius were widely dilated and full of clear fluid. There was no collapse of the cavities on drainage. The picture was one of internal hydrocephalus caused by a plastic meningitis occurring about the roof of the 4th ventricle obliterating the foramina of Luschka and Magendie, and of herniation of the cerebellum due to increased intracranial tension.

THE STOOLS IN CLINICAL SPRUE

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THE sprue syndrome is by no means a well-defined one, and shows many points of similarity to that seen in the chronic cases of dysentery and in multiple vitamin-B deficiency syndromes such as pellagra. The chief point of differentiation has been what is known as the sprue stool, characterized as pale, bulky, frothy, offensive, and of high fat content. The diagnostic usefulness of these criteria obviously depends on the constancy with which they occur in the sprue syndrome; and one of them, the 'fattiness' of the stool, can be scientifically applied only when fats can actually be estimated. The purpose of this investigation was to determine the incidence of 'characteristic' stools in sprue patients; and, from a practical point of view, to discover whether some simple procedure, such as microscopic examination of the stool, could take the place of chemical examination, which needs laboratory facilities not universally available in the tropics.

Material and methods.—A consecutive series of 150 stools sent to this laboratory for fat analysis has been examined. Over 90 per cent of these were from patients evacuated to the base as 'sprue', while the remainder were from patients with clinical features strongly suggestive

of sprue. The patients were kept on a 'sprue IV' diet, containing 70 gm. of fat, for three days before stool specimens were taken. The naked-eye appearance of the stools was noted, and a specimen examined microscopically for fatty-acid crystals, fat globules, and soap plaques. Total fat and split fat were estimated after acid hydrolysis and ether extraction of the dried stool in a Stokes' tube.

Results.—The figures for the analysis of individual stools are available for inspection in this laboratory. For brief presentation, the stools have been grouped in table I, which gives the number of stools with a fat content of less than 20 per cent, 20 to 30 per cent, 30 to 40 per cent, and over 40 per cent respectively. Only 28 stools out of 150 have a fat content of less than 20 per cent, even though the fat content of the diet was low.

Table I also shows the number of stools in each group which were pale. Since it is often paleness of the stools which leads to sprue being suspected, it becomes important to determine the relationship between fat content and pallor. For the relevant figures in table I, the value of χ^2 is 24.4, and the value of P less than 0.01; in other words, there is less than one chance in a hundred that the relationship observed between stool pallor and fat content is merely fortuitous. The relation between stool colour and fat content may be more easily seen from table II, which shows the incidence of paleness in stools of normal and abnormal fat content, taking 25 per cent as a commonly accepted upper limit of normal faecal fats. While 88 per cent of pale stools in this series have a total fat content of more than 25 per cent, the presence of pigment by no means excludes steatorrhœa, for 50 per cent of the abnormal stools were pigmented. The diagnosis of steatorrhœa cannot be made to await the appearance of typical pale stools. It is well recognized that paleness in a stool does not imply the absence of bile pigment, for it may be present in a reduced colourless form (Manson-Bahr, 1943); when the pale stools are treated with acid-alcohol for an hour or two, the alcoholic extract is well coloured. This is not the whole story, however, for in steatorrhœa the bulk of the twenty-four hour stool is much increased, and dilution of pigment contributes to the pallor.

Stool pallor and fat content are associated, but the figures also show that they are not completely dependent variables; for example, 38 per cent of the stools containing more than 40 per cent of total fat were pigmented.

Microscopical examination.—Fatty-acid crystals were seen in 55 of the 150 stools; while globules of neutral fat were seen in only three stools, and soap plaques in seven. The infrequent occurrence of fat globules in sprue as opposed to pancreatic steatorrhœa is worth stressing, in view of the fact that textbook illustrations of the microscopical appearance of

sprue stools generally include fat globules; but in the uncommon episodes of acute diarrhoea, fat globules may be seen in consequence of defective splitting due to intestinal hurry. Since fatty-acid crystals were by far the commonest microscopic abnormality, table III has been constructed to show the relation between the finding of fatty-acid crystals and the amount of fatty acids as determined by analysis. The value of χ^2 is 11.1 and of P 0.01, showing a significant association, crystals being seen more often as the fatty acid content of the stools increases. Table IV is a simpler expression of this relationship. Again, the absence of crystals cannot be taken as evidence that the stool is not a fatty one, for 61 stools out of 109 stools with a fatty acid content of over 20 per cent showed no crystals.

Discussion.—It is apparent that while steatorrhoea is found in the great majority even of isolated stool specimens from cases of clinical

sprue, it can only be detected with certainty in all cases by chemical examination. Out of 102 stools in which chemical examination showed a fat content of over 25 per cent, only 51 were definitely pale, and in only 46 were fatty acid crystals detected. Even taking both these criteria into account, only 68 of the 102 stools would have been suspected of being fatty without chemical examination. While pallor of the stool or the finding by microscopy of fatty-acid crystals is very suggestive of steatorrhoea, the absence of either or both of these characters cannot be taken to indicate the absence of steatorrhoea. Such a statement as this 'The estimation of neutral fat, fatty acids, and soaps by laborious laboratory methods is not necessary. The presence of excessive fat in the stools can be recognized by microscopical examination alone' (Cook, 1944) must certainly lead to error.

Summary.—Chemical analysis for total and split fat has been carried out on 150 consecutive

TABLE I

Numbers of stools grouped according to fat content; relation of total fat content to pallor

Total fat content (percentage of dry weight) ..	Less than 20	20-30	30-40	Over 40	TOTAL
Number of stools	28	38	48	36	150
Number of pale stools	5	8	20	26	59
Number of pigmented stools	23	30	28	10	91
Percentage of stools which are pigmented ..	82	79	58	38	61

TABLE II

Relation between fat content and pallor

Total fat content (percentage of dry weight) ..	Less than 25	More than 25	TOTAL
Number of pale stools	8	51	59
Number of pigmented stools	40	51	91
Total	48	102	150

TABLE III

Numbers of stools grouped according to fatty-acid content; relation of fatty-acid content to the finding of fatty-acid crystals microscopically

Fatty-acid content (percentage of dry weight) ..	Less than 20	20-30	30-40	Over 40	TOTAL
Number of stools	41	44	44	21	150
Number of stools without crystals	34	28	23	10	95
Number of stools with crystals	7	16	21	11	55
Percentage of stools with crystals	17	36	48	53	37

TABLE IV

Relation between fatty-acid content and the finding of fatty-acid crystals microscopically

Fatty-acid content (percentage of dry weight) ..	Less than 20	More than 20	TOTAL
Number of stools without crystals	34	61	95
Number of stools with crystals	7	48	55
Total	41	109	150

stools sent for fat analysis from patients with active, convalescent, or suspected sprue. Two-thirds of the stools examined had over 25 per cent of fat; pallor of the stool and the presence of fatty-acid crystals were commoner in stools of high fat content, but 34 out of 102 stools with increased fat showed neither pallor nor fatty-acid crystals. Chemical analysis is therefore needed to determine with certainty whether a stool contains an excess of fat.

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THE POSITION OF THE VERMIFORM APPENDIX

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THE vermiform appendix is notorious for the inconstancy of its position. With its base attached to the cæcum, it may occupy almost any position, like the hands of a clock, both in the sagittal and the coronal planes relative to the cæcum. This variability of its position is easily explained on the basis of an unequal development of the different parts of the original infantile cæcum. The appendix is first recognized when the proximal part of the cæcum grows out of all proportion to the distal end, which consequently retains its undeveloped form and lumen. At this stage the appendix must necessarily be attached to the lower end of the cæcum, in about its middle. The left half of the cæcum ceases to grow, or grows very little, while the right half grows enormously; this is the asymmetrical shape of the cæcum in the adult. The appendix which was, previous to this change, attached below at the junction of the right and the left halves of the cæcum, now appears to be attached to the left of the cæcum, because this junction has shifted to the left. Next, due to the rapid growth of the anterior wall of the cæcum as compared with the posterior, the appendix may be pushed gradually backwards behind the terminal ileum and cæcum (Wakeley, 1933). Thus, on the accelerated or retarded growth of the walls of the original cæcum depends the ultimate position of the appendix in the adult.

The various positions of the appendix were described by Treves (quoted by McGregor, 1943) by likening the appendix to the hand of a clock. Treves (Wakeley, 1933) thought that the splenic position in which the appendix

lies behind the terminal part of the ileum, with its tip directed towards the spleen, was the one met with in the majority of people, a view also shared by some modern authorities (Massie, 1944). Wakeley (1933) however held the contrary view, maintaining that the splenic position was the least common.

In table I are set out the results of analysis of a study of 591 appendices in Indians. Of these, 405 were seen at operation in cases of appendicitis in the Mayo and Sir Ganga Ram Hospitals, Lahore, and the rest (186) in the dead bodies used for dissection purposes in the dissection halls of the King Edward Medical College, Lahore, and the Dow Medical College, Hyderabad, Sind. The proportion of each of the various positions of the appendix are given in table II and compared with published results (Wakeley, 1933).

TABLE I

Position	591 APPENDICES IN INDIANS		
	Operation cases	Cadavers	Total
Anterior ileal ..	57 (14.1%)	12 (6.5%)	69 (11.7%)
Splenic ..	52 (12.8%)	40 (21.5%)	92 (15.6%)
Pelvic ..	33 (8.2%)	65 (34.9%)	98 (16.6%)
Subcæcal ..	15 (3.7%)	13 (7.0%)	28 (4.7%)
Retrocæcal and retrocolic.	248 (61.2%)	56 (30.1%)	304 (51.4%)
Total ..	405 (100%)	186 (100%)	591 (100%)

TABLE II

Author	PERCENTAGE OCCURRENCE OF VARIOUS POSITIONS OF APPENDICES				
	Anterior ileal	Splenic	Pelvic	Sub-cæcal	Retrocæcal plus retrocolic
Wakeley (1933).	1.0	0.40	31.01	2.26	65.28
Present authors (1945).	11.7	15.6	16.6	4.7	51.4

A glance at these tables will show that the results of analysis in Indians are in substantial agreement with those obtained in Europeans. The commonest position is the retrocæcal and retrocolic position (51.43 per cent), that is in the extremely developed type of cæcum where its anterior wall has developed so much more than the posterior as to have pushed the appendix behind the terminal ileum and behind the cæcum or the lower part of the ascending colon. Next in frequency in both Europeans (31.01 per cent) and Indians (16.58 per cent) is the pelvic type, where the appendix hangs over the pelvic brim or lies over the psoas

muscle. The splenic position does not appear to be so rare in Indians (15.56 per cent) as it is in Europeans (0.4 per cent). The anterior ileal position (11.67 per cent) and the subcæcal position (where the appendix lies below the cæcum, 4.73 per cent), make up the total.

Summary

A report is presented of 591 cases in which the position of the vermiform appendix was noted. Analysis of these cases confirms the view that the most common position of the appendix, in the adult, is the retrocæcal and retrocolic. The splenic position does not appear to be as rare in Indians as in Europeans.

Acknowledgment

We are indebted to the Medical Superintendent, Mayo Hospital, Lahore, for permission to consult some of the hospital records. Thanks are due, in particular, to Colonel P. B. Bharucha, Surgeon, Sir Ganga Ram Hospital, Lahore, for his kind permission to consult his operation notes, and to Professor M. A. H. Siddiqui, Head of the Department of Anatomy, King Edward Medical College, Lahore, from whose department some of the material was collected.

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4 : 4' DIAMIDINO-DIPHENYL-ETHER IN THE TREATMENT OF INDIAN KALA-AZAR

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4 : 4' diamidino-diphenyl-ether (phenamidine, M&B 736) is one of the series of aromatic diamidine compounds synthesized by A. J. Ewins. It was found to possess a marked curative action on *Babesia canis* infection by Lourie and Yorke (1939). Adler and Tchernomoretz (1942) tested the therapeutic activity of this drug in the treatment of infection by *L. donovani* in Syrian hamsters. They found that repeated injections of this drug in 10 mg. per kilo body weight doses did not control a mild infection in Syrian hamsters. Larger doses were not tolerated by these experimental animals. Wien (1943) studied the pharmacological action of this drug and found that phenamidine was the least toxic of the four diamidines—phenamidine, stilbamidine, propamidine and pentamidine; but the differences were not great. The least toxic had the least effect on blood pressure and the intestines. The metabolic changes produced by this drug were studied by Wien *et al.* (1943). Also the drug has been reported to be no more toxic on prolonged administration than pentamidine which has been found to be a relatively

non-toxic drug in the treatment of kala-azar and sleeping sickness.

A consignment of phenamidine was received in February 1944, and the immediate results of treatment of the first 16 cases were published by the writer in October (Sen Gupta, 1944). During that year, 30 cases in all were treated with phenamidine. The complete results of this therapeutic trial are presented in this paper. The immediate results of treatment, and also the results of follow up of the cases six months after they had been discharged as clinically cured, are discussed in this paper.

All the patients of this group, except two, were admitted into the hospital of the Calcutta School of Tropical Medicine. These two patients were treated at the kala-azar clinic of the school. Twenty-six of the patients were Indians, three Anglo-Indians, and one Chinese (the disease being acquired in Calcutta). The age distribution was as follows :

Between 1 and 10 years	8 cases
" 11 " 20 "	8 "
" 21 " 30 "	12 "
" 31 " 40 "	1 case
" 41 " 50 "	1 "
TOTAL	30 cases

The duration of illness varied from less than one month to 2 years. In 11 of the cases the duration was 2 months or less.

Twenty-eight of these patients were cases of ordinary untreated kala-azar and 2 were anti-mony resistant ('resistant') cases.

Diagnosis

The diagnosis in all cases was made on clinical grounds, confirmed by the aldehyde test and/or the complement fixation test with an antigen prepared according to the method of Witebsky, Klingenstein and Kuhn from the so-called leprosy bacillus of Kedrowsky (Sen Gupta, 1944a). Except in one obvious kala-azar case whose serum gave a strongly positive aldehyde reaction, *Leishmania donovani* was demonstrated in every case by sternal or splenic puncture. The aldehyde test was positive (+++, ++ or +) in 14 cases, (+) in 3, ± in 4 and negative in 7 cases. The complement fixation test was done in 29 cases; it was 'strongly positive' in 7, 'positive' in 21 and the serum was anti-complementary in 1.

Blood picture before treatment

A blood count was done in all cases on admission and at least once before discharge from the hospital, except in the one case of death. The mean value of hæmoglobin content was 8.1 ± 1.8 gm. per 100 c.cm. of blood, and the leucocyte count showed a mean of 2.96 ± 1.74 thousand per c.mm.

Treatment

The specific treatment with phenamidine was usually commenced after the usual hæmatological and parasitological investigations had

been completed. No accessory treatment beyond ingestion of glucose and alkalis was adopted. The complications that arose were treated symptomatically. The patients were usually on a full diet except when there was severe diarrhoea, dysentery, or high fever. Helminthic infection, if present, was treated well after the completion of treatment for kala-azar. Two cases showed malarial infection before the co-existing leishmaniasis was diagnosed, and these patients had anti-malarial treatment before the treatment for kala-azar. One of these cases has already been reported (Sen Gupta, 1944b). The treatment for anaemia by hæmatinics was postponed till after the treatment for kala-azar.

Route, routine and dosage

The drug was administered intravenously in all cases. Freshly prepared 1 per cent solution in sterile distilled water was used. The injections were given daily in almost all cases. The dosage scheme was more or less the same as in case of other diamidine compounds. The initial dose for an adult case of 'ordinary' kala-azar was 25 mg., and by increasing the dose daily by 25 mg., a maximum of 1 mg. per pound of body weight was reached in three or four stages, and this dose was continued till 10 injections were given. In children the initial dose was smaller, 10 to 15 mg., and the increase was by 10 to 15 mg. till the maximum of 1 mg. per pound of body weight was reached.

It was soon found out that one course of ten injections was not enough to produce a clinical cure. It was then decided to repeat the course of injections after an interval of ten days. Thus an average 'ordinary' case received two courses of 10 daily injections each with ten days' interval between the courses, the whole course taking a month. If within a fortnight of the completion of the second course of injections the patient did not show evidence of clinical cure, a third course of ten injections was given. In one 'resistant' case two courses of 15 daily injections with ten days' interval were given, and in the other the usual course for ordinary cases.

Though the scheme of injections was more or less uniform, the total dose of the drug given in each case varied widely. For the ordinary cases, excluding two cases, who did not complete the course of injections and one who died after receiving a few injections, and the 'resistant' cases, the mean total dose works out to be 1.73 gm. with a standard deviation of ± 0.477 gm. and the mean total dose per 100 pound body weight 1.854 ± 0.396 gm.

Reactions

The injections did not produce any marked immediate reactions except slight flushing and burning sensation over the face and the trunk in a few cases. These were very much milder than those encountered with other diamidines.

No toxic sequel like 'diamidino-stilbene neuropathy' was encountered within six months of completion of treatment; no case developed peripheral neuritis as reported after prop- amidine.

A small number of patients complained of slight discomfort over the liver region during the course of injections; this symptom subsided without any treatment except ingestion of glucose, and did not lead to any other complication. One child developed toxic jaundice after 30 injections of the drug; this cleared rapidly under symptomatic treatment. The epistaxis occurring in one case could not be ascribed to this drug, as this complication is not uncommon in kala-azar untreated, or during treatment with pentavalent antimonials.

Results of treatment

Fever.—As with other diamidines, the fever usually came down to normal within a few days of the completion of the first course of injections. In a few cases the temperature came down to normal within a week of commencement of treatment.

In one case the patient developed malarial fever during the course of injections of phenamidine. It therefore seems unlikely that this drug has any anti-malarial action.

Spleen.—The spleen did not show any signs of reduction in size during the first course of injections, but about the beginning of the second course some degree of reduction was appreciable. In the cases that responded to treatment, the spleen showed a well-marked reduction in size within a fortnight of completion of the second course of injections, and an enlargement up to 4 inches usually disappeared. From the following table showing an analysis of the size of the spleen before and after treatment, it will be evident that except in the three cases who failed to respond to treatment, in most cases the splenic enlargement was almost entirely relieved.

Size of the spleen before and after treatment

Degree of enlargement, inches below tip of 9th rib	Number of cases before treatment	Number of cases after treatment
0	0	9
0 to 1	3	13
1 to 2	8	2
2 to 3	7	0
3 to 4	3	1
4 to 5	3	1
5 to 6	2	0
Over 6	2	1
	28	27

There was progressive improvement of the general condition during and after the course of specific treatment of the patients who did not develop any serious complications, such as dysentery or pneumonia. Any oedema that was present subsided before the completion of the

first course of treatment, and after that the patients generally put on weight.

Weight

Increase by 7 lb. or less	..	11 cases
" between 7 lb. and 14 lb.	..	12 "
" " 14 lb. and 21 lb.	..	2 "
Weight remained the same	..	2 "
TOTAL	..	27 cases

Blood picture

There was usually very little improvement of the hæmoglobin and leucocyte count within a fortnight of commencement of the first course of injections. About a fortnight after the completion of the second course of injections the blood count showed well-marked improvement in all the cases that responded to treatment. The mean hæmoglobin per 100 c.cm. of blood after treatment was 11.5 ± 2.1 gm. and the mean leucocyte count was 7.05 ± 2.75 thousand per c.mm.—both showing well-marked improvement over the initial values.

Failures

In three cases (out of 30) phenamidine failed to produce a clinical cure. Two of these cases were antimony resistant cases, and the third, a moribund case that ultimately made what may be called a 'resurrection' after a stay in the hospital of three months and a half, during half of which period she hovered between life and death. She ultimately recovered after a course of stilbamidine, repeated courses of hæmatinics, and a blood transfusion.

Of the two 'resistant' cases, one case (with patent interventricular septum and tuberculosis of the right lung) improved considerably with phenamidine but did not make a clinical recovery; the fever came down to normal but the splenic enlargement and the blood picture did not show sufficient improvement and, even after two months, leishmania could be found in the spleen puncture smear. The patient was ultimately cured with three courses of injections of stilbamidine. This case has already been reported by Chakravarty (1945).

The other 'resistant' case also became apyrexial after phenamidine, but no improvement of blood count and splenic enlargement was apparent. She was later cured after a course of urea stibamine, followed by hæmatinics and treatment for latent malaria.

Death

One patient died. This was an Indian boy of thirteen years of age who was admitted in a moribund state after only four months of illness. He was extremely emaciated, asthenic and anæmic. There was complete loss of voice, and signs of bronchitis over both lungs. Three days after the commencement of treatment, the patient had hæmoptysis and developed dysphagia in addition to aphonia, and the general condition steadily grew worse. He did

not respond to the symptomatic treatment that was adopted, and died suddenly a week after admission. No post-mortem examination was allowed. It seems likely that the patient had a cancrum-like process involving the larynx and the upper respiratory tract.

Immediate clinical cures

Of the thirty patients treated, two did not complete the course of injections and were later treated with antimonials leading to clinical cure. The remainder, 28 cases, had one or more courses of 10 daily injections. Of these 28 cases, 24 were discharged as clinically cured, 1 patient died, and in 3 cases the drug failed to bring about a cure. These patients were subsequently treated with other drugs and discharged cured (*vide supra*). The immediate cure rate lies between 74 and 98 per cent, the mean being 86 per cent.

Final results

The 24 patients who had been treated with phenamidine alone and discharged as clinically cured were followed up 6 months or more after the completion of their treatment. Three cases could not be traced (two were 'destitutes'), five cases relapsed and were treated with antimonials, and 16 cases were either seen to be in good health or replied stating that they were in good health, free from fever and enlargement of the spleen, and that they did not require any more specific treatment. These 16 cases can be regarded as permanently cured for all practical purposes (*cf.* Napier, 1932). The permanent cure rate is 64 ± 19 per cent, *i.e.* it lies between 43 and 83 per cent.

Of the 5 cases which relapsed, one had been discharged as clinically cured after only 10 injections and he relapsed within 2 months of discharge from the hospital. The other cases however had full courses of treatment, but they relapsed within 2 to 4 months.

Conclusions

4:4' diamidino-diphenyl-ether has a fair degree of curative action on Indian kala-azar. On statistical consideration of the data of this obviously small series of cases, it can be concluded that both the immediate clinical cure rate and the final results are inferior to those obtained with the most effective pentavalent antimony compounds, or with diamidino-stilbene.

Usually two courses of 10 daily injections, each separated by an interval of 10 days, are required to produce a clinical cure, the whole course requiring a month (as with the urea stibamine group of drugs, the injections being given on alternate days).

The compound can be used in the treatment of selected cases of kala-azar, particularly those exhibiting intolerance to the antimonials and those complicated with grave pulmonary conditions such as pulmonary tuberculosis. It is a

relatively non-toxic drug and does not produce any serious complication during the course of treatment or any sequelæ.

Acknowledgment

The writer is thankful to Messrs. May and Baker, Ltd., Dagenham, England, and their local representatives for placing at his disposal a very generous supply of phenamidine for the purposes of this investigation. To Dr. C. Chandrasekhar, M.Sc., Ph.D. (Lond.), thanks are due for advice regarding the statistical evaluation of the data.

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[Note.—The complete details of the 30 cases here reported were recorded in a table which has been omitted from this article to save space.—Editor.]

PROTEIN HYDROLYSATE IN INFECTIVE HEPATITIS

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THAT hydrolysed proteins could be safely given intravenously to protein-starved animals was first shown by Henrique and Andersen (1913). Elman and Lischer (1943) administered large amounts of amino-acids and peptides intravenously to men without any ill effects. They were able thus to maintain nitrogen equilibrium in patients who could not take food by mouth. Bassett *et al.* (1944) report a study of a patient with gastro-jejuno-colic fistula, who was given solutions of amino-acids intravenously and subcutaneously, without clinical disturbance and with satisfactory maintenance of nitrogen equilibrium. Krishnan and others (1944) stimulated by the famine conditions in Bengal in 1943 prepared hydrolysed proteins for parenteral administration in starvation cases.

The method of preparation was explained and shown to me by Professor Krishnan at the Institute of Hygiene, Calcutta. The enzyme used for protein hydrolysis is papain which is supposed to contain both proteinase and polypeptidase. Papain acts optimally at pH 5 to 7 and at a temperature of 50°. Papain is produced easily by collecting the latex of the unripe fruits of *Carica papaya* after scarifying the fruits while still on the tree. By mixing the latex with acetone and drying it repeatedly, an active preparation of papain in powder form can be obtained. Pork which is freed from all fat and bones is minced to a fine consistency. 1/40 by

weight of papain dissolved in water is added to it. The digestion is conducted at 50°C. for 24 hours. The extent of digestion is then tested by determination of the formal titre, total solids and total nitrogen. The undigested proteins and metaproteins, which are usually small in amount and which are likely to produce anaphylactic reactions, are removed by heat coagulation at pH 7. 'During the process of preparation, bacterial contamination is avoided through the use of an aseptic technique and a preservative (toluol). The final product is mixed with glucose and sodium chloride so as to give a mixture containing 5 per cent protein hydrolysate, 5 per cent glucose and 85 per cent sodium chloride. The mixture is then sterilized and tested before issue, biologically in the cat for toxicity, bacteriologically for sterility, and immunologically for allergic reaction.' Krishnan emphasized that the potency and efficacy of the preparations depend chiefly on the freshness of the meat used, absolute sterility, and the removal of reaction-producing protein molecules by heat coagulation.

Hydrolysis of protein by papain is not complete, so much so that the final product obtained is a mixture of polypeptide and amino-acids. It contains methionine as well, though not in such quantities as one finds in casein hydrolysate. Analysis of the mixture has shown that it contains also riboflavin, nicotinic acid and thiamin.

Samples of protein hydrolysate were given to me by Professor Krishnan for trial in January 1944, and later further supplies as were necessary.

My experiences with protein hydrolysate are mostly in the treatment of infective hepatitis. It was the studies of Himsworth and Glynn (1944) on the rôle of protein deficiency in the genesis of hepatic disorder, and the experiences of Beattie and others with the use of casein digests in the treatment of carbon tetrachloride poisoning, that stimulated me to try protein hydrolysate in cases of infective hepatitis. Owing to the difficulty in procuring large supplies at any one time, the trials had to be spread over a period of 9 months. Each time a trial was made, however, proper controls were selected, with due consideration to the date of onset, the degree of jaundice and the severity of toxic symptoms.

Fifty-four cases were studied for the purpose of assessing the value of protein hydrolysate; 27 were treated with the protein digest, while the remaining formed controls. Fifteen cases were treated during the middle and later months of 1944, while 12 were treated in a batch during February and March of this year. All the samples that were supplied to us were prepared during the early months of 1944. That might account for the better results obtained last year as compared to the results obtained in the 12 cases treated this year. Being a biological product it might have undergone deterioration by keeping.

Two hundred c.c. of protein hydrolysate with a pint of glucose saline were given by intravenous drip. In the first 6 cases, 800 c.c. of the hydrolysate were given over a period of 4 days. In 7 cases, 600 c.c. were given and in the remaining only 400 c.c. were given. In every case the number of days taken for the restoration of appetite, for the improvement of general condition, for the urine to become pigment free, for the conjunctiva to be free from icterus and for the liver to become normal in size were noted. In the majority of the cases, weekly estimation of icteric index and sedimentation rate were also done. Table I shows the average for the whole series of 27 cases with their controls. Table II shows the results in the last 12 cases contrasted with their controls. With the exception of the giving protein

TABLE I

Protein hydrolysate in infective hepatitis; first 27 cases

Since commencing treatment	Average for treatment, days	Average for controls, days
Appetite restored in ..	2.8	8.5
General condition improved in ..	3.0	7.5
Urine pigment free in ..	6.8	12.8
Conjunctiva clear in ..	10.1	14.3
Liver normal in ..	10.4	21.4

TABLE II

Protein hydrolysate in infective hepatitis; last 12 cases

Since commencing treatment	Average for treatment, days	Average for controls, days
Appetite restored in ..	5.0	9.0
General condition improved in ..	5.1	8.0
Urine pigment free in ..	13.0	13.5
Conjunctiva clear in ..	15.8	16.0
Liver normal in ..	16.4	20.4

hydrolysate, all cases and their controls were treated exactly on the same lines. In spite of the results obtained in the last 12 cases being not so striking, owing possibly to the stock being old, the treated series of all the 27 cases have a better average than the control series. Restoration of appetite, and improvement in the general condition, are strikingly quick in the treated series. Even after the first infusion, the patient experiences a sense of well-being. As regards the disappearance of jaundice however, the results have not been uniformly striking. In the first series of 15 cases, in 8 cases bile disappeared from the urine within 5 days of the beginning of treatment. The average in the whole series of 27 cases is however not as good as was expected. The time taken for the

icteric index to come to normal was almost the same both in the treated and in the untreated series. The sedimentation rate took a longer time to come to normal in the control series than in the treated series. In the majority of cases of infective hepatitis, the sedimentation rate begins to rise by the end of the 2nd week, reaches maximum in the 4th week and comes down to normal by the 7th or 8th week. On the average the sedimentation rate in the treated series becomes normal in the 6th week.

Another good result obtained in the treated series is the greater rapidity with which the liver comes to normal size. That protein constituents are needed to prevent liver necrosis has been shown by the experiments of Himsworth. When digestion is impaired, parenteral administration of predigested protein is the method of choice. Marked improvement in the general condition noticed in the treated series is evidently due to the direct supply of the protein requirements of the body and the re-establishment of nitrogen equilibrium. Protein digests have a protective action on the undamaged portions of the liver.

It is not possible to say whether they have any favourable action on the damaged cells or not, as improvement so far as icterus is concerned is not striking. A much larger number of series have to be studied before a definite opinion is given on that matter.

From the observations made on the treated series, the following conclusions have been drawn:—

1. Protein hydrolysate has definitely a place in the treatment of cases of infective hepatitis with toxic symptoms.
2. Vomiting disappears and appetite is restored very quickly.
3. The liver becomes normal within a shorter period.
4. The degree of jaundice is not appreciably affected in the majority of cases, though in the first few cases striking results were obtained.
5. The sedimentation rate comes down to normal in a shorter time.
6. Better results are given in those treated early. Hence I am inclined to believe that if the treatment is instituted in the pre-icteric or the early icteric stage the results will be more favourable.
7. A more extensive trial should be made before one can say that it helps to shorten the period of hospitalization.

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SULPHANILYL BENZAMIDE IN THE TREATMENT OF BACILLARY DYSENTERY

(A PRELIMINARY NOTE)

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SINCE the introduction of sulphaguanidine by Marshall *et al.* (1940), many papers have been published reporting the clinical use of this compound in the treatment of intestinal infections, particularly bacillary dysentery. Its efficacy has been attributed to its powerful bacteriostatic action and its high local concentration in the bowel as a result of poor intestinal absorption. But the drug has certain drawbacks. Vomiting is sometimes caused after its administration and symptoms such as rashes, nausea, headache, tachycardia and fever are not infrequently found (Smith, 1944; Brewer, 1943). Moreover, the dosage is unusually large (Clay, 1943) and thus the cost of treatment is necessarily high. Moreover, sulphaguanidine is found to be ineffective against Sonne dysentery (Fairbrother, 1944).

Brownlee and Tonkin (1941), experimenting *in vitro*, reported the bacteriostatic action of sulphanilyl benzamide against dysentery bacilli to be more than that of sulphaguanidine. Bose and Ghosh (1944) have noted a low toxicity associated with a better absorption of this drug in mice and rabbits. In view of these previous findings, it was considered to be of interest to study the effect of this compound in the treatment of bacillary dysentery. Accordingly, a trial of sulphanilyl benzamide was given to a small number of indoor patients of this hospital.

In selecting patients, histories were taken, thorough clinical examinations, total and differential blood counts and blood examinations for parasites were made; stools were examined macroscopically and microscopically with cultures on McConkey's plates (certain ingredients necessary for desoxycholate agar were not available). In the selection of cases chief stress was laid on the typical macroscopic appearance of the bacillary dysentery stool.

Details of cases and results of treatment.—Nineteen cases were treated. They all showed very numerous stools before treatment, containing blood and mucus. About half of them were febrile and half were not. Some showed marked dehydration, and some showed signs of malnutrition. The stools of all of them were characteristic of bacillary dysentery. Cultures of the stools were done in 14 out of the 19 cases; in only 4 was the pathological organism isolated, 3 being Sonne organisms and the 4th being Flexner. Two patients died, one early in the treatment. In the remaining 17 cases, the

number of days before a normal stool was passed varied between 3 and 7. Except the two who died, all patients made a clinical recovery. No toxic effects attributable to the drug were seen. The dosage of the drug used was 2 tablets three times a day for the first few days and later twice a day; the length of treatment varied between 4 and 7 days according to the time when the stool became normal.

The drug concentration in the blood two hours after drug administration, generally on the second day of treatment, was estimated in 7 cases.

TABLE I

Drug concentration 2 hours after drug administration on the 2nd day of treatment

Case number	CONCENTRATION OF DRUG IN MG. PER 100 C.C.M. OF BLOOD		Percentage of conjugation
	Free	Total	
1	2.94	2.94	Nil
2	6.80	8.80	22.7
3	10.00	12.50	20.0
4	Nil	Trace	
5	6.90	7.70	10.4
6	2.20	3.10	29.0
7	2.80	3.80	26.3

Discussion

All the cases except two responded to the treatment by sulphanilyl benzamide. In none of the cases was there any toxic manifestation in spite of its fairly high systemic absorption (*vide* table I). The average number of days required for a clinical cure, as judged by the passage of formed stools without blood or mucus, was found to be 4.6. Of the 2 patients who died, one survived only a few hours after admission and had had only 4 tablets of sulphanilyl benzamide; the other was in a devitalized condition caused by prolonged malnutrition.

These findings tend to establish the fact that the drug sulphanilyl benzamide is certainly beneficial in the treatment of bacillary dysentery. Bacteriologically positive Sonne and Flexner cases have definitely responded to this treatment. In this connection, it may be noted that Swyer and Yang (1945) have also observed with this drug effective bacteriological clearance of organisms in Sonne cases. The average clearance observed by them was 1.8 days for this drug whereas with succinyl sulphathiazole it was 2.4 days, with the highest relapse rate. The findings from this hospital are in good agreement with theirs.

It remains however to study the effect of this preparation on Shiga dysentery, on the carrier state of patients, and controls treated with other

sulpha drugs before a final assessment of the value of this drug can be made.

In conclusion we beg to express our indebtedness to Drs. N. Ali, H. Roy, the late Dr. Ali Ahmad, M. L. Chakravarty, and S. Bhattacharya of the Campbell Medical School for their very helpful suggestions and for help with the laboratory part of the investigations. We also acknowledge with thanks the liberal supply of sulphanilyl benzamide from Bengal Immunity Co., Ltd., required for these investigations.

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JAUNDICE IN AMOEBIC LIVER ABSCESS

A REPORT OF TWO CASES

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FROM a survey of available literature, latent jaundice appears to be not uncommon in amoebic hepatitis and abscess of the liver, but deep jaundice is a very rare accompaniment.

Reference to this combination is also absent or meagre in textbooks of pathology and in most of the commonly used textbooks of tropical diseases. Rogers and Megaw (1942) record in their book on tropical medicine one case from Calcutta. Manson-Bahr (1939) in his book on dysenteric disorders quotes Cope (1920) referring to jaundice in tropical liver abscess. Rolleston and McNee (1929) quote Moir (1902): 'Jaundice is very rarely deep. More commonly a condition of latent jaundice with tinging of the conjunctiva is present. In exceptional cases an abscess may press on the extrahepatic ducts in the portal fissure'. Kirkaldy-Willis (1942) from Kenya records two cases of obstructive jaundice with stenosis of bile ducts.

Because of the rarity of case reports of jaundice in liver abscess, there seems to be an impression in the minds of medical students and practitioners that the presence of deep jaundice negatives a diagnosis of amoebic liver abscess. During the course of our autopsy examinations in the Medical College, Madras, we came across

two cases of liver abscess with jaundice within a period of two years (1943 and 1944), and we thought it desirable to report them.

Case 1.—Mr. A., a Christian male of 48 years, was admitted into the General Hospital for fever and pain in the epigastrium of 15 days' duration with jaundice for 10 days. There was no previous history of diarrhoea or dysentery. The left lobe of the liver was enlarged and tender.

The following findings were made on investigation: bile pigments in the urine, no bile salts and no leptospira; no malaria parasites in the blood; red blood cells $3\frac{1}{2}$ millions, white blood cells 8,400, polymorphs 75 per cent; van den Bergh direct immediate strong positive.

The patient died at the end of a week and a partial post-mortem examination was conducted within an hour of death.

On opening the abdomen, the stomach and intestines were seen distended, and the omentum congested. The peritoneal cavity contained deeply bile-stained turbid fluid. Sub-diaphragmatic exploration revealed a rent in the upper surface of the liver through which chocolate-coloured pus was pouring into the peritoneal cavity. The diaphragm was intact and there were no sub-diaphragmatic adhesions.

The liver showed a thickened capsule with wrinkling in places. A sagittal section running through the abscess showed congestion and bile-staining of the entire parenchyma, with evident peri-portal fibrosis. There was a thick fibrous walled oval abscess, 4 inches \times $3\frac{1}{2}$ inches, in the right lobe (figure 1, plate XVIII) extending from the superior surface, where it had ruptured, to $\frac{1}{2}$ inch from the inferior surface, and pressing at its lower pole on the right hepatic duct which was embedded in fibrous tissue. The contents of the abscess were necrotic. Sections made from the wall of the abscess close to the hepatic duct showed vascular fibrous tissue with diffuse infiltration and focal aggregations of lymphocytes and histiocytes, a markedly dilated, tortuous large bile duct, collections of bile capillaries (figure 2, plate XVIII) with inflammatory cell infiltration around and non-medulated nerve bundles were seen in the wall. Further out, the liver cells showed fatty change with inspissation of bile, and in the sinusoids distension with diffuse round cell infiltration. There was peri-portal fibrosis with extension into the parenchyma. Numerous amoebae were seen amidst the necrotic contents of the abscess (figure 3, plate XVIII).

Case 2.—R. N., a male of 30 years, was admitted into the General Hospital on 5th February, 1944, for pain in the jaw, jaundice and distension of the abdomen with a complaint of pain in the liver area from the day previous to admission. Examination revealed a readily bleeding tumour in the gum of the second molar tooth extending into the cheek, enlarged and hard submental and submandibular glands and ankyloglossia.

The urine showed bile pigments and salts. Rectal examination showed nothing particular. The case was diagnosed as carcinoma of the cheek with metastases in the liver. The patient died on 16th February, 1944. Post-mortem examination revealed the following:—There was deep jaundice with necrosis of the left side of the upper jaw and inflammatory induration of the tongue. The heart showed a flabby myocardium with patchy pericarditis on the right ventricle. The lungs showed pleural adhesions, oedema and congestion. There was a diffuse peritonitis. The bile-stained liver (5 lb.) was enlarged and revealed on sagittal section, three honey-combed abscesses in the right lobe (figure 4, plate XVIII), a small circular one 1 inch in diameter situated $\frac{1}{2}$ inch from the superior surface and 1 inch lateral to the attachment of the falciform ligament, and two large oval abscesses, each 3 inches \times 2 inches, one of these extending to a quarter of an inch from the superior surface and the other into the quadrate lobe, pointing towards the duodenum. There

were adhesions between the duodenum, gall-bladder and the quadrate lobe, involving the common bile duct. The walls of all the abscesses were ragged and the contents necrotic. The duodenum showed inflammation and necrosis of the mucous membrane at the junction of the first and second parts. Sounding with a probe revealed a block in the lumen of the common bile duct proximal to the sphincter of Oddi. The stomach showed a partially healed ulcer $\frac{3}{4}$ inch in diameter along the lesser curvature near the pyloric end. The gall-bladder was thickened and opaque, and had an area of acute inflammation in the body. There were healed and active ulcers in the most dependent portion of the caecum. The other viscera were congested. Under the microscope the walls of the abscesses were seen formed by compressed and elongated liver cords, the individual cells being atrophic, with inspissated bile. Sinusoidal congestion and round cell infiltration were seen. Further away from the abscesses, whose contents were necrotic with a few leucocytes and numerous amœbæ, the picture was the same, with the usual cord and lobular pattern not prominent.

Comment.—In case 1, a malignant growth of the liver and gumma were thought of, but not amœbic abscess, and likewise in case 2, secondary metastases in the liver, since the patient had an epithelioma in the cheek. It would appear that in neither case were the fæces examined because the nature of the condition was not suspected in the least. The purpose of this article is to emphasize that in tropical countries hepatomegaly with jaundice should suggest the possibility of an amœbic abscess in common with other toxic, degenerative, inflammatory and neoplastic conditions. A routine examination of fæces for the vegetative and cystic forms of *Entamoeba histolytica* is of paramount importance, since coincidental hepatic and colonic lesions are common in our experience. In a series of ten complete autopsies of liver abscess we performed, associated intestinal lesions were seen in six. A diagnostic aspiration should be done unhesitatingly, since the material obtained can in any case be utilized by the pathologist for a histopathological examination, to decide upon the nature of the malignant growth, if the material is not amœbic pus.

The sub-icteric tinge seen in amœbic hepatitis is due to the impaired function of the liver cells, the cause of toxic jaundice. It will be appreciated from our case reports that deep jaundice can occur only in obstruction to the main bile ducts, but may be found in acute as well as in long-standing abscesses, the mechanism of obstruction being different in the two instances. In an acute abscess with ragged walls as in case 2, the tension in the abscess is not likely to reach the level at which pressure on the main bile ducts would be exerted and cause jaundice, since necrosis can spread further, a factor which will contribute to the size of the abscess but not to pressure. What then could produce obstruction to the bile ducts? It is the peri- and intra-ductal inflammation which produces partial or complete obstruction. On the other hand, in a long-standing abscess with a thick fibrous wall, the tension inside the abscess is bound to be high, and

pressure on a main bile duct should cause jaundice of an obstructive type.

The question then arises as to why jaundice is such a rare accompaniment though tropical abscess is by no means uncommon. We feel that the occurrence of jaundice is primarily influenced by the situation of an abscess and the nature of its wall and least by its size. This would explain the absence of jaundice in abscesses which are very large but situated on the antero-superior aspect. Mere destruction of liver parenchyma, as is seen in portal cirrhosis, does not cause jaundice, as there is a great reserve of excretory power. When 95 per cent of the liver has been destroyed, the surviving 5 per cent is capable of preventing jaundice.

Summary.—Two cases of jaundice in tropical liver abscess are reported.

The pathogenesis of jaundice is discussed, and examination of fæces as a routine is recommended in every case of hepatomegaly with jaundice.

The diagnostic utility of aspiration biopsy is emphasized.

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A NEW TECHNIQUE IN STERNAL PUNCTURE

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and

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A KNOWLEDGE of the changes in the bone marrow has become indispensable in the diagnosis of various blood diseases and protozoal and bacterial infections in the tropics. In the year 1903, Wolff obtained the marrow from the medullary cavities of tibia and femur by open operations. Just about the same time, Pianesi (1903) aspirated bone marrow from the long bones after puncturing with Potain's apparatus. Ghedini (1908) was the first to trephine the upper end of the tibia and curette the marrow. For nearly two decades, this method was extensively used. Seyfarth (1923) simplified the technique by trephining the sternum instead of the tibia. However, this method of investigation was not very widely

practised, since sternal trephining involved the care of a surgical operation. Arinkin (1929) simplified the technique by puncturing the sternum with a stout needle and aspirating a mixture of blood and bone marrow. Subsequently many modified types of needles have been devised for sternal puncture (Arieff, 1931; Baserga, 1934; Weller, 1937). Salah's needle (1934) made on similar lines is in common use in this country.

The superiority of sternal trephining over puncture is accepted by all, since the marrow aspirated by the latter method is always diluted with blood. It is generally agreed that the greater the volume of fluid aspirated, the greater is the admixture with blood. By comparing trephine and puncture methods on the same case, Jeannert showed that in the aspirated fluid the more immature cells and megakaryocytes are not always included. Since aspirated material contains variable quantities of blood, enumeration of leucocytes, nucleated red cells, erythroblasts and megaloblasts, has given inconsistent results. At times, the variations are so great that the figures add nothing of value to the data. To overcome this, Henning and Korth injected heparinized plasma through the puncture needle before aspiration, and claimed withdrawal of marrow elements without a mixture of blood. However, in routine examination of smear preparations of bone marrow, the disadvantages of sternal puncture are outweighed by the ease and simplicity of the technique.

The purpose of the present communication is not to enter into a detailed comparison of the two methods and their relative merits, but to describe a new technique, introduced by the senior author, whereby the simplicity of sternal puncture is retained and the disadvantage of dilution eliminated.

The new sternal puncture needle (figure 1) employed in this technique is a steel rod (gauge .44) 2 inches long, with a deep vertical gutter in its last $\frac{3}{4}$ inch, and a bevelled tip, fixed to a thick handle. The left wall of the gutter is higher than the right, and its edge is sharp, so that when the needle is rotated clockwise while inside the medullary cavity, the marrow is scraped and the gutter filled. A section of the needle across the gutter is shown in (figure 2).

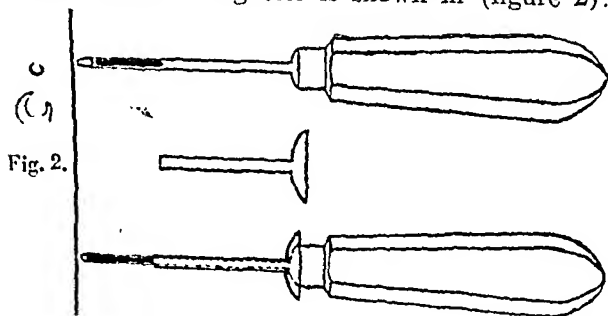


Fig. 1.—Reddy's sternal puncture needle with the shield.
Fig. 2.—Section of the needle across the gutter, lower one magnified.

A cannula or shield made of thin steel encloses the needle up to the upper end of the gutter.

Procedure.—The needle is sterilized and freed from moisture. The skin, subcutaneous tissues and underlying periosteum of the sternum opposite to the 3rd or 4th intercostal space are infiltrated with novocain. The needle is inserted vertically halfway between the midline and the lateral margin of bone. It is then tilted until it makes an angle of about 30° with the surface of the skin (figure 3). With a screwing side-to-side movement, the anterior plate of the

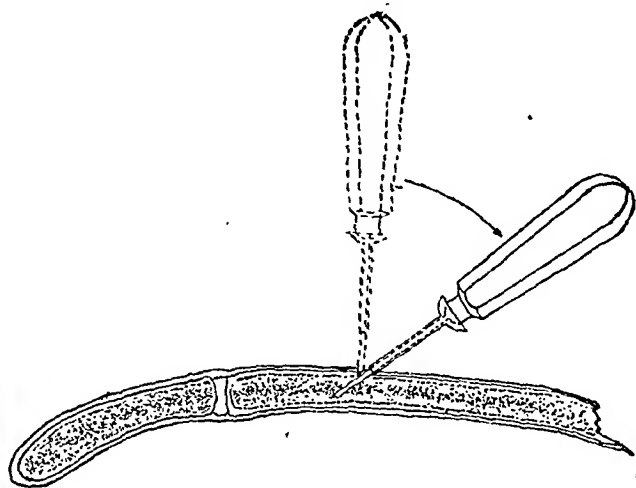


Fig. 3.—Diagram showing the position of the sternal puncture needle inside the sternum.

sternum is penetrated, and the needle pushed 1 cm. deep. When the bevelled surface of the needle is kept facing downwards, it should travel parallel to the surface of the sternum. When the needle has been driven to the required depth, the guard should have travelled through the entire thickness of the soft tissues and have just penetrated the periosteum. The advantage with the oblique puncture is the elimination of the danger of mediastinal penetration even when 2 cms. of needle is pushed into the sternum. (If desired, the needle can be used for a vertical puncture also.) The needle is now rotated once or twice clockwise and withdrawn with the guard *in situ*. This protects the marrow from being wiped off the needle by the soft tissues during withdrawal. Enough solid marrow can be scraped out of the gutter with a needle to make half a dozen smears. These have to be made very thin, as otherwise there will be overcrowding of cells and individual cells cannot be distinguished. When it is desired to culture the marrow for pathogenic organisms, the marrow from the gutter can be inoculated into appropriate media by removing it with a sterilized platinum loop.

We have used this needle extensively on cadavers and later on anæmic and kala-azar patients admitted into the General Hospital, Madras. The advantages we claim are:—

1. The operative technique is very simple, involving the handling of a single instrument.

2. Bone marrow undiluted with blood is invariably obtained, whereas with aspiration, occasionally dry punctures may result or only blood be withdrawn.

3. Smears made from the marrow show sheets of cells with their anatomical relations undisturbed. Both immature cells and megakaryocytes are seen in large numbers (figure 4, plate XVIII).

4. In kala-azar, numerous parasitized cells are found unruptured, thus saving time in the search for parasites.

While carrying out the above investigation, we have made the following additional observations:—

1. We have punctured the body of the sternum opposite to the 3rd and 4th intercostal spaces and also the manubrium in the same patients and found the smears identical. According to Pässler (1931), the manubrium is less suited for puncture since aplasia occurs earlier than in the body, and the spongiosa is often thin in the centre (Lissitzyn, Arieff). Our observations made on a number of sternums longitudinally sawn are not in complete agreement with the above. We recommend puncture of the manubrium in all children, in thin and emaciated individuals and in adults in whom the skin over the body of the sternum is unhealthy.

2. We have also measured with callipers the thickness of the bared sternum in the middle line corresponding to 1st to 5th intercostal spaces. The average measurements were 10.7, 10.4, 9.3, 9.2, and 9.5 mms., opposite to the 1st, 2nd, 3rd, 4th and 5th, intercostal spaces respectively. The safe distance a needle can be pushed by the oblique method which we advocate is 15.0, 14.9, 14.0 and 14.3 mms. respectively. Other advantages with the oblique puncture are (1) it is easier to push the needle in, (2) no stop is necessary since there is not the remotest chance of penetration into the mediastinum, and (3) bone marrow over a long distance is included in the specimen removed. The pain and discomfort experienced by the patient are in no way greater than with the vertical puncture.

We are at present engaged in a study of the total and differential counts of marrow removed by this method in normal individuals. According to Segerdahl (1935), nucleated cell counts in aspirated bone marrow of healthy men are 75,000 per c.mm. with a variation of 38,400 and in women 82,700 per c.mm. with a variation of 24,100 per c.mm. Greif (1937, 1938) has recorded that the counts vary from 45,000 to 150,000 per c.mm. These figures show that the counts hitherto published are very variable, and these variations, even after providing for the lability of bone marrow, are mostly due to dilution with blood (figure 5, plate XVIII). We feel confident that with our technique, errors due to the second factor can be eliminated. Preliminary counts done with marrow removed from the cadavers in accidental deaths reveal a higher percentage of immature cells.

The differential counts as published to-day are again at variance and unsatisfactory, as the leucocytes of the admixed blood are necessarily added to the cells of the marrow. This naturally results in inflation of the leucocytic count and an incorrect myeloid-erythroid ratio from which granulopoietic and erythropoietic activity can be judged. It should be possible to enumerate the cells more accurately in future, since undiluted marrow is obtained with the present needle.

The use of this needle has been demonstrated at a clinical meeting of the General Hospital, Madras, on 28th July, 1945. At present the instrument is in use in almost all the wards of the institution, and the consensus of opinion is that it is very satisfactory and superior to Salah's needle.

Summary

A new sternal puncture needle to obtain undiluted bone marrow with ease is described. The needle is simple in construction, unlike Salah's needle, and dispenses with suction with a syringe. The advantages and superiority of the new technique in the study of bone marrow are pointed out. Immature cells and megakaryocytes are found in greater numbers; Leishman-Donovan bodies in kala-azar are detected with ease; total and differential counts of both myeloid and erythroid cells in the marrow can be carried out correctly, since dilution with blood is eliminated.

I have to thank Lieut.-Colonel G. R. McRobert, I.M.S., former Professor of Medicine, Medical College, Madras, and Physician, General Hospital, who encouraged me in my hæmatological work, and the Superintendent and Physicians of the General Hospital for facilities afforded to me to perform sternal puncture on patients under their care.

I am extremely grateful to United Surgical Works Ltd., a local surgical instrument manufacturing company, Mount Road, Madras, for making the needle to my design. It may be obtained from them.

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[The author of this paper has been good enough to send to us one of these needles for trial. Owing to difficulty in obtaining suitable steel, the preparation of these needles has apparently been a little difficult; if suitable steel is not used, the canalated needle is not strong enough and may break during use, the broken needle being difficult to remove. The firm mentioned supplied one needle, and then asked for it to be returned and supplied another apparently made of better steel.—EDITOR. I.M.G.]

ACUTE MENINGITIS, SOME IMPRESSIONS

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(Based on the paper read before the XV Annual Mysore Medical Conference, Bangalore)

THIS paper is an attempt at recording briefly my impressions on the subject and is based upon the observations made on 37 patients that came under my care from January 1944 to June 1945.

The ætiological classification as suggested by Brain (1940) is adopted. Though the incidence of the several varieties of acute meningitis has been established in western countries, I have been unable to lay my hands on any such records for this country, though a few workers like Gour (1943), and Law and De (1944) have now and then mentioned the cases they had to deal with.

Acute aseptic meningitis is an important member of this family. This condition has been attributed to a virus by workers like Baird, Rivers and MacCallum. I had to deal with 19 cases of acute meningitis where the ætiological factor could not be established either by the microscopic or cultural methods. As the cerebro-spinal fluid in these cases conformed to the description given of the fluid obtained in aseptic meningitis, it is presumed that these cases were of this variety. If this assumption is correct, acute aseptic meningitis is the commonest variety of acute meningitis we are called upon to deal with in these parts. This impression will have to be sustained by further observations.

Symptoms and signs.—Fever, headache, vomiting, photophobia, delirium, convulsions and coma are the usual symptoms met with, one variety presenting one particular symptom more markedly than the other. In only one case of meningococcal meningitis was there no fever; only one case developed petechial rashes. The mental state tended towards hyperpsychomotor activity in all the types except the tuberculous type where it tended towards lethargy and coma.

Except for nuchal rigidity, a positive Kernig's sign, frequently a unilateral or bilateral squint; altered pupillary reaction to light and rarely extensor plantar response, there were not many signs in evidence. Taranto (1943) also mentions the paucity of neurological changes in his series of cases.

Course and prognosis.—The outlook in the aseptic type is the most satisfactory. All the cases which came under my observation recovered by the end of a week or so. In the other varieties I had to deal with, i.e. 5 meningococcal, 4 pneumococcal and 4 mixed pyogenic cases, there was only one death, and this was in a case of pneumococcal meningitis. The outlook in the tuberculous variety has remained as

gloomy as ever. The five cases which came under my observation either died in the hospital or were discharged from the hospital in a moribund state.

Diagnosis.—It is in the field of diagnosis that much care has to be exercised. While the recognition of the pyogenic variety does not give rise to any difficulty, as the cerebro-spinal fluid is characteristic, and microscopic or cultural examination of the fluid clinches the diagnosis, the recognition of the acute aseptic variety gives some difficulty. This is because various conditions like meningism associated with acute infectious fevers, serous meningitis following a cranial focus of infection, acute serous meningo-encephalitis, cerebral malaria and tuberculous meningitis resemble one another clinically. Thus, in all these conditions, the patient comes to the doctor with a history of fever and headache. On examination, signs of meningeal irritation are found. On doing a lumbar puncture, the cerebro-spinal fluid is found to be usually clear and under pressure, while a microscopic examination of the fluid shows in all cases a mononuclear pleocytosis and a negative culture. Gour (1943) has dealt adequately with this subject. I will only deal with the differentiation of aseptic meningitis from cerebral malaria and tuberculous meningitis.

Acute nervous symptoms frequently occur in falciparum malaria. Viswanathan (1944) and Bhattacharjya (1945) have referred to this subject and have quoted some typical cases. Whatever the histopathology of cerebral malaria may be, signs of meningeal irritation are frequently associated with it. Cerebral malaria as a condition to be differentiated from acute meningitis is a frequent problem in this country. Diagnosis is easily and quickly established in most cases by an examination of a thick or thin blood smear. Hunter (1945) and Bhattacharjya (1945) have said that the parasite could be demonstrated in almost all cases. My experience has also been similar. But it does happen very occasionally that a case resembling acute meningitis has to be treated as a case of cerebral malaria on the grounds of the patient's residence in the endemic area, the history of previous attacks of malaria and the finding of an enlarged spleen though the parasite cannot be demonstrated in a blood smear. It has happened that in such cases the administration of 5 gr. of quinine intravenously immediately and sometimes repeated after, has resulted in quick improvement in the patient's condition. Reddy (1945) has referred to a similar case. I have on record 5 cases of fever and unconsciousness where a diagnosis of cerebral malaria was presumed and quinine administered. In four of them consciousness returned in 6 to 12 hours and the temperature touched normal within a day. Only one died after about 18 hours. While it is not scientific to administer quinine as a specific measure in the

absence of a definite diagnosis, and it is necessary to conserve our quinine supply in these days of scarcity, in some rare instances we shall have to relax in our attitude and administer quinine on mere clinical grounds, as cerebral malaria is one of the diseases where deterioration in a person's condition sets in very rapidly, and timely administration of quinine may be the only thing that could improve matters.

It is best to quote the words of Brain when dealing with the differentiation between acute aseptic meningitis and tuberculous meningitis, as the former belongs to the same subgroup as acute lymphocytic choriomeningitis and resembles it clinically in every detail. 'Acute lymphocytic choriomeningitis is likely to be confused with the tuberculous meningitis, and since the absence of the tubercle bacillus from the cerebro-spinal fluid cannot be held to exclude the latter, the two conditions may be indistinguishable until the recovery of the patient settles the diagnosis in favour of the benign disorder.' If it is possible to establish the diagnosis early, it will be possible to make an accurate prognosis, recovery or death. The following table indicates the essential differences between these two diseases:—

origin has been suggested. These cases are characterized by an acute pulmonary infection, resembling clinical lobular pneumonia; the mortality is low, physical findings minimal, radiograms characteristic, complications few except meningo-encephalo-myelitis.

Cerebro-spinal fluid shows pleocytosis with preponderance of lymphocytes, a slight increase in protein content and a negative culture; the condition does not respond to any sulpha drugs but runs a benign course, the temperature regaining normal by lysis in 7 to 15 days. As in some cases of acute aseptic meningitis which have come under my observation, I have found signs of pulmonary involvement also, I feel that there is something in common between them and the cases of atypical pneumonia described by Sheppe and Reimann.

Treatment.—The problem becomes simple where treatment is concerned. A lumbar puncture and examination of cerebro-spinal fluid will decide whether it is a case of pyogenic meningitis or aseptic meningitis. Serum therapy, sulpha drugs, penicillin are very beneficial in the former type and should be administered early and in adequate quantities. The choice of the drug depends upon the conveni-

		Lymphocytic choriomeningitis	Tuberculous meningitis
1	Age	Any age	Usually 2 to 10 years.
2	Onset	Always acute	Usually insidious.
3	Fever	High continuous	Low remittent.
4	Course	Fever comes down by lysis in about a week or two.	Fever continuous until death which comes on by 2 to 3 weeks.
5	Mental state ..	Tends towards hyperpsychomotor activity.	Tends towards lethargy or even coma.
6	General physical condition ..	Wasting not marked, toxic manifestations pronounced.	Emaciation always present specially if complicated with pulmonary tuberculosis. Toxic manifestations mild.
7	Signs of meningeal irritation	(i) Nuchal rigidity severe (ii) Headache, mild (iii) Photophobia variable	(i) Nuchal rigidity mild. (ii) Headache, intense. (iii) Photophobia always marked.
8	Lung signs ..	Signs of acute pneumonitis may sometimes be present if lungs are involved, but not of consolidation or cavitation.	If lungs are involved, signs of caseation and cavitation are present indicative of extensive damage to lungs.
9	W.B.C. ..	Normal or leucopenia	Moderately high.
10	Eye grounds ..	Rarely congestion is present	Fundal changes are fairly frequent, e.g. congestion of disc (papilloedema and choroidal tubercles may be present).
11	Pirquet's test ..	Has no significance. May or may not be positive.	Usually negative.
12	Cerebro-spinal fluid	Usually clear, may rarely be turbid, always under increased tension, moderate pleocytosis of mononuclear cells; protein content increased, glucose and chloride content normal. No 'cobweb' forms on standing. No tubercle bacilli present. Tryptophane not present.	Always clear and never turbid, always forms 'cobweb' on standing, high pleocytosis of mononuclear cells, protein content increased, chloride content very low, i.e. 500 mg./100 c.cm. Tubercle bacilli demonstrable in the web and tryptophane present. Guinea-pig inoculation proves the condition.

Recently, workers in America like Sheppe and Reimann have been reporting cases of atypical pneumonia with a secondary involvement of the central nervous system for which a virus

ences available. As I have used penicillin in only a few cases I have not been able to estimate the relative merits of these drugs. Repeated lumbar punctures and symptomatic

treatment are all that are necessary in aseptic meningitis. In tuberculous meningitis no treatment is of any use.

Summary.—Certain impressions gathered while treating 37 cases of acute meningitis are recorded. The incidence and symptomatology of the different forms are briefly outlined.

The differential diagnosis of acute aseptic meningitis from cerebral malaria and tuberculous meningitis is mentioned in detail.

A common virus origin for acute aseptic meningitis with pulmonary involvement and atypical pneumonia with involvement of central nervous system is suggested. Treatment is briefly discussed.

In conclusion, I wish to acknowledge my debt of gratitude to Drs. C. Krishnaswamy Rao and T. Seshachalam for permitting me to utilize the clinical material of the hospitals under their charge and to the several house physicians who have assisted me in the investigation of the above cases.

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THE TREATMENT OF KALA-AZAR WITH SODIUM ANTIMONY GLUCONATE (STIBATIN). FURTHER OBSERVATIONS ON THE TREATMENT OF THIRTY-TWO CASES

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Introduction.—Burke and Chakravarty (1944) published a preliminary report of twenty-one cases of Indian kala-azar treated with sodium antimony gluconate, antimony-hexonate or 'Stibatin' (Glaxo Laboratories). Every case of that series showed all-round improvement, resulting in immediate clinical cure. As the criterion of clinical cure is very misleading with this disease, these cases were followed up and kept under observation for a period of six months after completion of the course to ascertain if there was complete or 'protozoological' cure as well. Out of these twenty-one cases, three cases relapsed within six months while the others remained healthy; giving 14.28 per cent relapse and 85.72 per cent cure rates respectively. In view of these encouraging results, it was decided to undertake

a further extensive trial with this drug in certain hyperendemic kala-azar areas in the tea districts of Mangaldai, as an anti-kala-azar drug of such promising quality was indispensable, especially when, due to present war-time conditions, other pentavalent antimony compounds of proved value, e.g. solustibosan, neostibosan, etc., suitable for mass administration, disappeared from the market. Sodium antimony gluconate in the earlier part of its clinical trials in the treatment of kala-azar, by certain workers in India, failed to produce full therapeutic results, the chief reason attributable being presumably inadequate dosages. The only statement on record so far available on its failure has been made by Napier and Sen Gupta (1943), who state that in three of their cases treated with this compound, there was no effect in one case and slight improvement but no cure in the other two cases. There is however no mention about the dosage employed by them. From all-round clinical experience of the first series of twenty-one cases treated last year, the dosage scheme laid down by the makers, i.e. 60 c.cm. of the solution (containing 20 mg. of the Sb compound per c.cm.) proved insufficient for an adult to effect a cure, and this was safely and accordingly increased to a total dose of 150 c.cm. (15 c.cm. daily for ten days). It was also advocated that, in certain selected cases, a total dose of 200 c.cm. in ten injections should be given and that such a dose was without any toxic manifestations; this appeared to be the most appropriate maximum dose suggested with this compound in India. Kikuth and Schmidt (1943) advocated a total dose of 120 to 180 c.cm. for a course, but they were of the opinion that a total dose of 240 c.cm. could be administered without any toxic reaction. Patel in successfully treating his six cases of kala-azar in Bombay with this drug, used 20 c.cm. daily for ten days in some of the cases. In Chinese kala-azar, Chung *et al.* (1942) claimed successful results with a total dose of 60 to 162 c.cm. of the solution. From the above reports, it is evident that sodium antimony gluconate has been used in varying doses by different workers. To derive optimum therapeutic results, and to find out a more suitable dosage scheme easily applicable for a maximum effect with this compound, a series of thirty-two confirmed cases of kala-azar was taken up for further experiment, and the detailed analytical findings are recorded below. These results, it is believed, warrant publication. Sodium antimony gluconate is a definitely potent pentavalent compound at our disposal, easily procurable in the present day.

Analytical findings of the cases.—All the cases of this series were admitted for treatment in two tea estate hospitals in the Mangaldai tea districts.

Race.—All were Indians, of whom 29 were tea garden labourers and the other three were middle class people.

Age distribution.—The age distribution was as follows :—

TABLE I

Range of age, years	Number of cases	Average age, years
1 to 10	3	5.0
11 to 20	6	13.6
21 to 30	9	25.3
31 to 40	10	36.8
41 to 50	4	45.0
TOTAL	32	

Sex.—Of the total 32 cases, nineteen were males and thirteen were females.

Duration of illness.—Duration varied from about two weeks to five months, the average of all cases being 2.14 months.

Diagnosis.—Diagnosis was confirmed in all cases (except cases 1, 4, 8 and 10) by the demonstration of *Leishmania donovani* in the spleen or sternum puncture smear. Diagnostic puncture of cases 1, 4, 8 and 10 could not be done because of the objection of the patients, but a definite diagnosis was arrived at by clinical symptoms, changes in the blood, and serological tests. In addition every case was thoroughly investigated with systemic examinations and other tests, i.e. the aldehyde test, Chopra's antimony test, total and differential counts of blood, etc.

Hæmoglobin level.—Due to lack of facilities for more accurate hæmatological technique, Talqvist's hæmoglobin scale was used for estimating hæmoglobin level before and after treatment. The findings were as follows :—

TABLE II

Per cent of hæmoglobin (Talqvist's scale)	Number of cases before treatment	Number of cases after treatment
30 to 40	4	Nil
41 to 50	19	Nil
51 to 60	9	10
61 to 70	Nil	20
71 to 80	Nil	2

Average hæmoglobin level of all cases before treatment was 49.0 per cent.

Average hæmoglobin level of all cases after treatment was 65.0 per cent.

Difference (gain) after treatment was 16 per cent.

Treatment.—There were a few cases which may be considered as very advanced or complicated, the maximum duration of illness being five months; the other cases were mainly of two weeks to three months' duration. Except in one case no treatment had been given before. Prior to commencing the specific treatment, almost all cases received a course of anthelmintic treatment, and complications such as bacillary dysentery, amoebic dysentery,

hepatitis, etc., were treated. Diarrhoea and other associated complications were dealt with by therapeutic measures along with the specific treatment. Stibatin was administered intravenously in every possible instance in varying initial doses to detect immediate reaction, if any, after the first injection. Injections were also given at any time of the day, irrespective of full or empty stomachs.

Dosage.—From previous experience of the preliminary work done with this drug (Burke and Chakravarty, 1944), the total dose was estimated according to age, i.e. 150 to 200 c.cm. were given to the majority of adult cases weighing 100 lb. and over. In children below 15 years of age, 1 c.cm. per year of age multiplied by ten was estimated as the total dose for a course of treatment. The course was completed in ten injections, with a smaller initial dose, and the maximum was reached by gradual increase. More than ten injections were also given in a few unusually resistant cases and in those in which delayed toxic action was detected. At the same time no attempt was made to follow the above dosage scheme very strictly in every case, and variations also occurred in the duration of treatment in a few cases. The principal idea of doing so, was to secure accurate data for a more suitable dosage scheme for both a 'clinical' and 'protozoological' cure together. Table III shows the average age, weight and doses received in this series of cases.

TABLE III

Age range, years	Number of cases	Average age, years	Average weight, lb.	Average total dose received, c.cm.
1 to 10	3	5.0	32.0	49.0
11 to 20	6	13.6	75.5	92.5
21 to 30	9	25.3	102.5	169.0
31 to 40	10	36.2	106.6	160.0
41 to 50	4	45.0	104.0	175.0
TOTAL	32	27.34	93.7	112.0

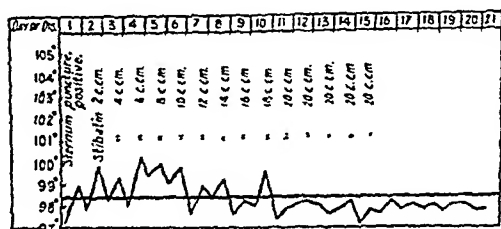
Result of treatment

Immediate reaction.—There was no systemic reaction immediately after injection in any of the patients, except in one patient who experienced palpitation after the first injection.

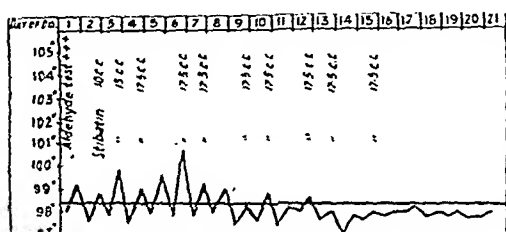
Delayed reaction.—In two cases, albuminuria developed, after four injections in one case and after seven injections in the other. Specific treatment was suspended till the urine was free of albumen, and the maximum dose was repeated again to complete the course. Subsequent albuminuria did not occur, and the patients were cured.

Fever.—The fever subsided in most cases before the end of the course of treatment or when three-fourths of the total dose had been

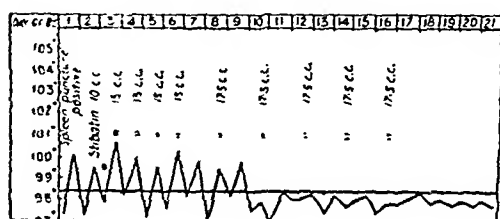
administered. The earliest period for the temperature to decline was seven days. In some resistant cases the temperature dropped on completion of the course. Temperature charts from 8 typical cases are annexed.



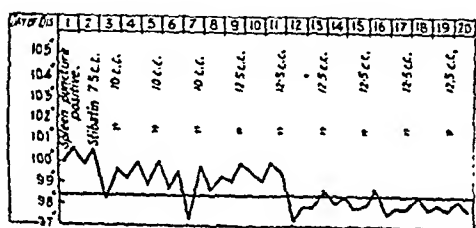
Case 2. Chart 1.



Case 10. Chart 2.

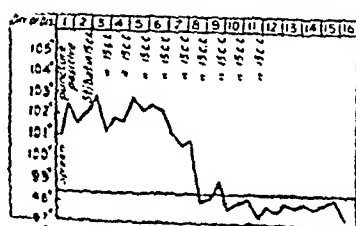


Case 16. Chart 3.

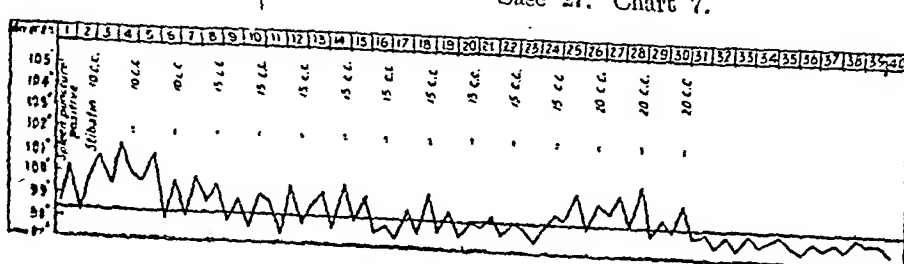


Case 17. Chart 4.

Spleen.—In most cases the spleen progressively became softer and smaller by the middle of the course. In a few cases, however, the enlargement of this organ remained quite unaltered till the end of the course; after which it gradually became softer and was reduced in size. On an average, there was a reduction of 2.87 fingers in the spleen measurement.



Case 18. Chart 5.



Case 28. Chart 8.

Improvement in general condition and other clinical features

Except in those who had complications at the time of admission, there was progressive improvement during and after the course of treatment. Such associated complications as oedema, diarrhoea, etc., began to subside gradually after a few days of treatment. There was gradual increase in weight, except in three patients with dropsy, whose weight diminished with the disappearance of oedema. Table IV shows the average weight before and after treatment.

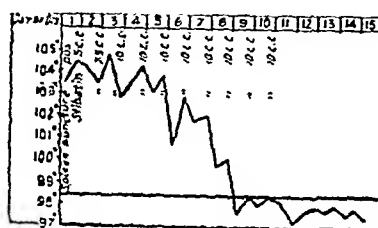
TABLE IV

Average weight before treatment	Average weight after treatment
93.7 lb.	100.3 lb.

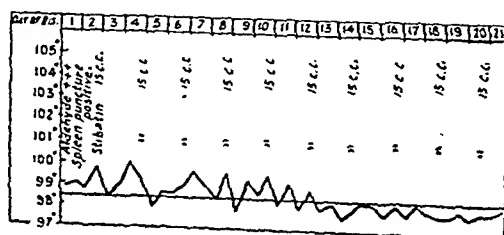
Difference (gain) after treatment was 6.6 lb.

Hæmoglobin.—There was an increase of 16 per cent (\pm deviation 2.5 per cent approx.) after completing the course of treatment (*vide supra*, table II).

Blood picture after treatment.—In almost all the cases, leucocytosis was observed after the course of treatment. The serum of cases giving a strong aldehyde reaction before commencing treatment gave weak positive or negative results after the course. Spleen or sternum puncture was done in 18 cases after treatment, and no *Leishmania donovani* were found in the smear.



Case 25. Chart 6.



Case 27. Chart 7.

Dosage.—From table III, it is evident that a patient with an average weight of 97.3 lb. received a total dose of 112.0 c.cm. or 2.240 grammes of Sb compound for a course, and from this figure it was found that 100 lb. of body weight would require a total dose of 125 c.cm. (2.5 grammes of Sb compound) approximately or 1.25 c.cm. of the solution per lb. of body weight. If the adult cases on the other hand are separately analysed (*vide supra*, table III), it appears that higher doses were required in proportion to body weight which works out roughly at 1.50 c.cm. or 30 mg. of Sb compound per lb. of body weight.

Failures.—In the whole series there was no case which did not respond to treatment. One case required a proportionately higher dosage, as it was found to be a resistant one. On following the cases up to six months of completion of the course of treatment, two cases were found to have relapsed.

Discussion

Criteria of cure.—All the patients of this series, except two who relapsed, have been keeping good health after six months of treatment, giving a 93.75 per cent cure rate and 6.25 per cent relapse. These results are very gratifying and prove conclusively that the drug has undoubtedly effected both a 'clinical' and a 'protozoological' cure with the dosage described. According to Napier (Napier, 1926-32; Napier *et al.*, 1937), the pioneer worker on this subject in India, the criterion of complete cure has been indicated by the time after completing a course of specific treatment, and he is of the opinion that if a case relapses, it does so within six months of the completion of the course. From the above findings, it appears very justifiable to conclude that sodium antimony gluconate possesses a well-marked anti-kala-azar property if administered in appropriate doses (*vide supra*) for a complete cure, and also with the evidence presented above, it appears that it has many advantages over the other pentavalent compounds, especially where a mass treatment is necessary. It will not be out of place to mention in this discussion that recent chemotherapeutic researches have advanced kala-azar therapy by the introduction of synthetic aromatic diamidines, and reports have been published of the excellent results obtained from these preparations from abroad. As far as Indian kala-azar is concerned, these drugs, 4:4 diamidino-diphenylethylene (M.&B. 744) and 4:5 diamidino-diphenoxy-pentane (M.&B. 800) have been experimented with in a small group of cases of visceral leishmaniasis (Napier and Sen, 1940; Napier and Sen Gupta, 1943). These non-antimonial preparations have not been advocated for general use due to unpleasant alarming reactions, in the majority of cases, experienced immediately after administration of the drug, and also due to neuropathic sequelæ in

some cases (Napier and Sen Gupta, 1942). The relapse rate with the latter drug M.&B. 800) is much higher (12 relapse out of 30 cases) than with pentavalent compounds (Sen Gupta, 1944). An editorial in the *Indian Medical Gazette* (1943) states as follows:

'It will be evident that, as far as India is concerned, the large majority of ordinary cases of kala-azar will continue to be treated and cured with pentavalent antimony compounds.' So, for the present, let this be with Stibatin.

Conclusion.—From experimental findings of thirty-two cases of genuine kala-azar, sodium antimony gluconate (antimony-v-hexonate) or Stibatin, has been found a specific drug in the treatment of Indian kala-azar; the toxicity of this compound is remarkably low compared with other pentavalent antimony compounds. In tea-estate practice, especially in hyper-endemic kala-azar areas under present economic conditions occasioned by the war, where the institution of mass treatment is necessary, it is very essential to have a drug of such a quality, *viz.*, which is not toxic, highly effective and easily and safely administered (either intramuscularly or intravenously). From all-round experiments with this drug, one can safely advocate *standardizing* the total dose at 1.50 c.cm. of the solution or 30 mg. of the Sb compound per pound of body weight for a course of treatment. The total dosage may be divided into ten injections to be given daily, or every alternate day, starting with smaller initial doses and the maximum being reached gradually. In patients of higher weight, where the total dose is estimated as more than 200 c.cm., the number of injections may be increased, and no attempt (in the writer's opinion) should be made to exceed 20 c.cm. of the solution for a single injection. This dosage scheme should vary in resistant cases, as, in such cases, one course of treatment should not be considered sufficient, and occasionally a more intensive treatment may be required. In uncomplicated cases, the duration of treatment should not exceed two to three weeks.

Acknowledgments

The writer is highly grateful to Dr. G. C. King, Medical Officer, Mangaldai Medical Association, for his kind permission to publish this paper. Special thanks are due to Dr. J. R. Lahiri for conducting treatment of a few cases and to J. K. Das Gupta for all his help and technical assistance in the investigation. Finally, deepest gratitude is due and heartily accorded to Messrs. H. J. Foster & Co., Ltd., Bombay, agents for Glaxo Laboratories in India, for their generous supplies of Stibatin *gratis* for the experiment.

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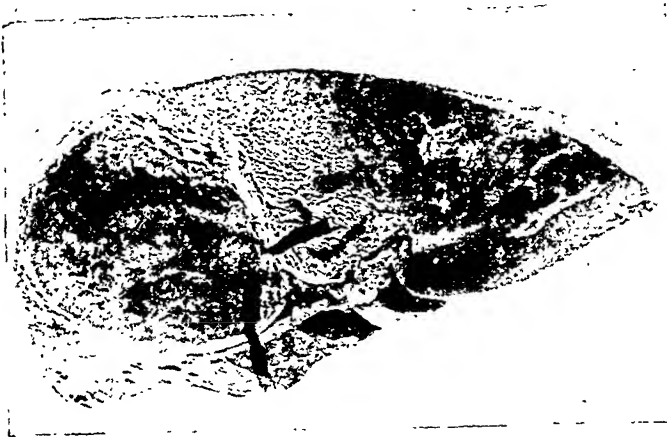


Fig. 1.—Sagittal section of the liver in case 1, showing a solitary abscess with thick fibrous wall pressing at its lower pole on the right hepatic duct.



Fig. 2.—Low power photomicrograph of a section made from the wall of the abscess proximal to the occluded bile duct showing dilated tortuous bile ducts surrounded by fibrous tissue and inflammatory cells.

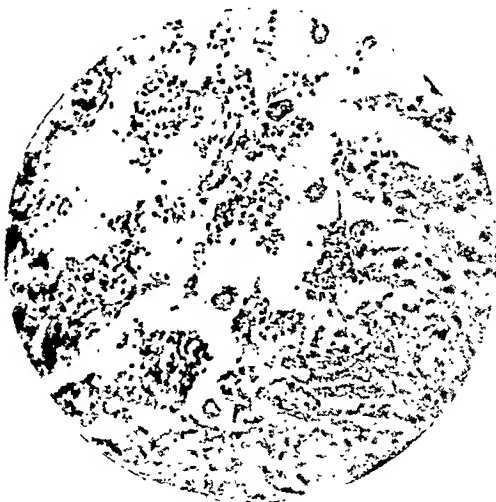


Fig. 3.—Medium power photomicrograph of a section made from the necrotic material inside the abscess showing amoebæ.



Fig. 4.—Sagittal section of the liver in case 2, showing honey-combed abscesses in the right lobe. The posterior aspect of the anterior half of the liver is shown in the photograph.

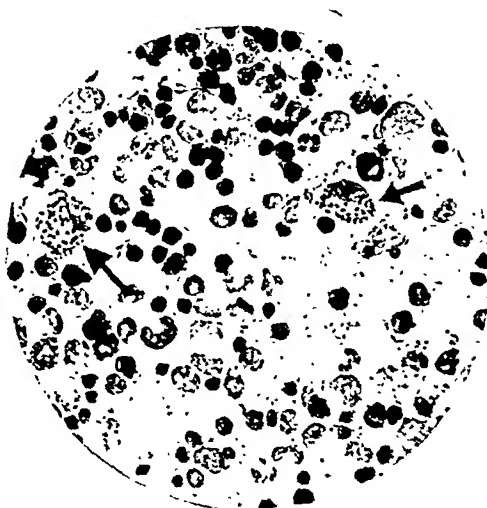


Fig. 4.—Photomicrograph of smear preparation of sternal bone marrow obtained with Reddy's needle. Marrow cells are found in large numbers with very few red blood cells. Two entire cells loaded with Leishman-Donovan bodies are seen. Stained with hæmatoxylin and eosin. X 500.

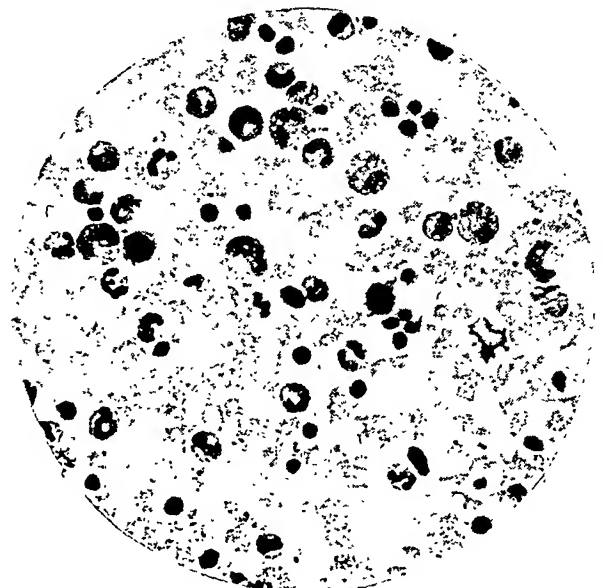


Fig. 5.—Photomicrograph of smear preparation of sternal marrow obtained with Salah's needle. Note marked dilution with red blood cells and sparse immature cells. Stained with hæmatoxylin and eosin. X 500.



Fig. 1.—Photograph showing the condition before treatment.



Fig. 4.—Photograph showing the result after treatment.

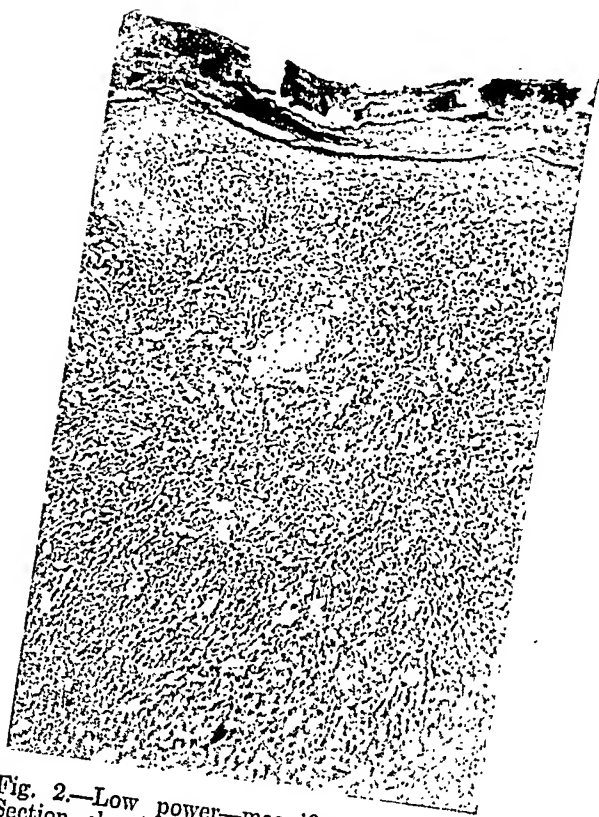


Fig. 2.—Low power—magnification $\times 100$. Section showing dense infiltration in the corium.

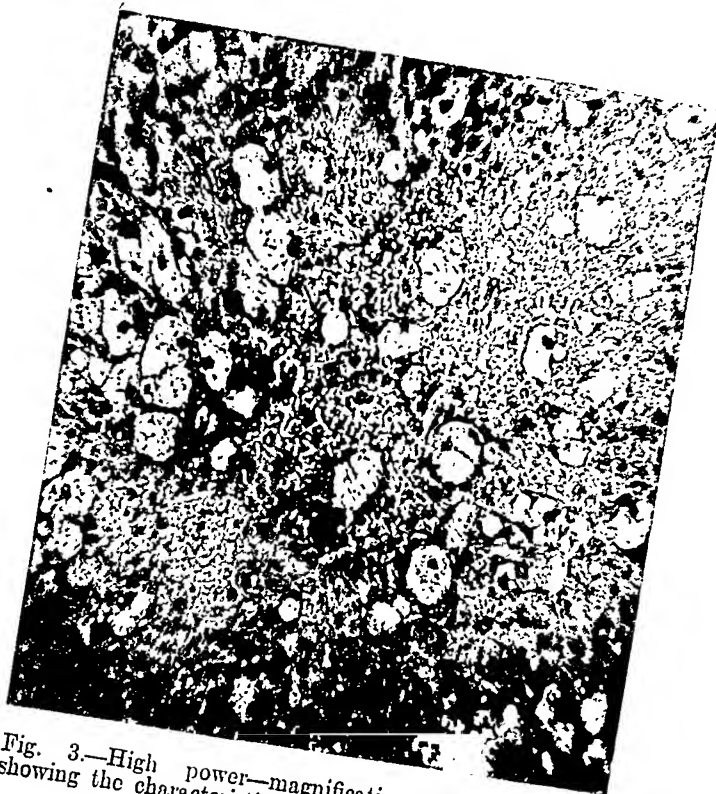


Fig. 3.—High power—magnification $\times 430$. Section showing the characteristic vacuolated cells, the mikuliez cells, in the infiltrated area.

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- Ibid.*, **79**, 49.
- [The manuscript of this article was accompanied by an enormous table of 32 columns, one for each patient, giving extremely complete details of all the patients, the treatment given, and the results. It is impossible, however, to publish this table.—EDITOR, I.M.G.]

A CASE OF RHINOSCLEROMA

By L. M. GHOSH, M.B. (Cal.), D.T.M. (L'pool) and

D. PANJA, M.B. (Cal.)

(From the School of Tropical Medicine, Calcutta)

T. H. A., MOHAMMEDAN MALE, aged 28 years, came to the out-patient department of the Calcutta School of Tropical Medicine for treatment of an ulcer of the nose and upper lip.

Examination.—A young man of good physique and health with no other ailments but the ulcer of the nose. The lower portion of the nose and the whole of the upper lip were involved into a hard fungoid growth. The surface of the growth was ulcerated with a foul smelling offensive seropurulent discharge. The hairs (moustache) were absent from the skin over the lesion. The openings of the nares were completely obstructed by a hard cartilaginous growth inside both the nostrils. The entire area was a hard sclerotic plaque adherent to the underlying tissue and ulcerated on the surface. On the tip of the nose there were some nodules—stony hard, not movable and continuous with the parent growth. The growth together with the ulcerated surface caused much disfigurement. The colour of the lesion was partly pinkish and partly whitish owing to the cicatrization. The growth was not painful, but was tender on pressure and the discharge was very offensive. Breathing was necessarily through the mouth owing to the obstruction in the nares (figure 1, plate XIX).

History.—He is a factory worker and acquired the disease in Calcutta. About 6 years ago the patient noticed a small nodule in the middle of the upper lip at the root of the nasal cartilage. The nodule was painless and freely movable at first; this gradually went on increasing in size and became a hard diffuse sclerotic plaque firmly adherent to the underlying tissues. Slowly the growth extended to the nose and the upper lip. After three years the growth on the nose and lip broke down with superficial ulceration and seropurulent discharge. For the last three years the patient had various treatments in different hospitals without any effect.

Clinical investigation.—The blood picture showed no abnormality. Kahn and Wassermann reactions were negative. The urine showed no abnormality. After a continuous application of warm normal saline compress changed every 3 hours for two days a nodule was slit open and the exudate was inoculated for culture. Smears were also made from this exudate for examination. Biopsy was also done for section.

Smear—Gram negative short bacilli were found arranged singly or in pairs; on further stain the bacteria were found enclosed in capsules.

Culture—primary culture on glucose agar media—small pinhead-size cream-coloured colonies.

Subculture on nutrient agar—the growth was gelatinous with tendency to settle at the bottom of the tube. The growth proved to be a pure culture of *Klebsiella rhinoscleromatis*.

Histopathology.—Epidermis: The epidermis was fairly normal but with localized collections of leucocytes and some parakeratosis. In some places the epidermis was stretched and the interpapillary processes flattened out as in atrophy.

Corium or dermis: The corium and the supporting tissues were practically replaced by dense granulo-matous infiltration. The cellular elements were chiefly plasma cells, some hyaline or colloidal degeneration of cells and peculiar large cells scattered throughout the infiltration giving the section the characteristic appearance. These Mikulicz cells are large, pale, swollen cells usually occurring in small groups. These cells contain clumps of the bacteria in the protoplasm. The infiltrate was compact giving rise to the firmness of the lesion; proliferation of the capillaries were absent (figures 2 and 3, plate XIX).

Treatment.—The ulcer was dressed twice everyday with a mild antiseptic lotion. Acriflavin lotion 1 to 5,000 and 2 per cent boric ointment were applied, and one full course of x-ray therapy was given, but the response was very poor.

He was then given a course of autogenous vaccine from the culture of the *K. rhinoscleromatis* and along with it another course of x-ray therapy. This time the response was quick and the recovery was uneventful (figure 4, plate XIX).

There remains however obstruction of the nares due to the cicatrization of the healed ulcer, and a plastic operation is proposed.

Discussion.—Rhinoscleroma is not very common in India although it is reported from time to time. In Bengal the disease is a rare condition, though a few cases have been seen in natives of Bengal who have never left the province. But there is no record in the literature of the occurrence of this disease in Bengal, and this is the first report.

DEEP REFLEXES IN NEURAL LEPROSY

By R. SUBRAMANIAM, M.D., M.R.C.P. (Lond.)
Medical Officer, Leprosy Department, Government General Hospital, Madras

This communication records a study of a group of cases of neural leprosy seen at the Government General Hospital, Leprosy Department. The cases under review showed the typical drop foot or claw hand or hands. The disease in all cases were clinically characterized by thickening of the peripheral nerves with definite anaesthesia, and nearly all showed simple macular anaesthetic patches in some part of the body. The writer elicited the knee jerk in some cases of drop foot and noted

the jerks to be brisk. In cases of peripheral neuritis by the time drop foot occurs the reflexes are lost completely. With a view to utilizing this sign as a differential diagnostic point a group of cases showing claw hands and drop foot were studied. In all the cases the deep reflexes on the affected side was very brisk. In one or two cases it was just brisk and in no typical case of neural leprosy were the deep reflexes poor or absent.

A few cases in which the deep reflexes were absent but showed claw hand were not suffering from neural leprosy but the claw hand was due to other causes.

In the available literature there is no reference to this fact that the deep reflexes are very brisk in advanced neural leprosy cases. The writer has tested the reflexes in the neural leprosy cases without any deformity and found them to be brisk. So this sign is valuable in cases which are fairly early and a definite diagnosis cannot be made by demonstration of bacilli and in which the clinical signs are equivocal. Cervical rib for example produces claw hand, but the biceps and supinator jerks are feeble or absent.

The ankle jerk in all the cases of leprosy with drop foot was present. The biceps and supinator jerks were brisk in cases showing claw hands. It is a well-known fact that the deep reflexes are exaggerated in the early stages of peripheral neuritis when the case is supposed to be in the irritative stage. The irritants in the peripheral nerves are lepra bacilli and they, being present all the time, keep up the irritant even when the patient develops drop foot and this, I believe, is the cause of the exaggeration of the deep reflexes in leprosy. It is very difficult to demonstrate the bacilli in every case because the bacilli are too few in the peripheral nerves, but probably this much is sufficient to cause exaggeration of the deep reflexes. The exaggeration of the deep reflexes does not seem to bear any relation to the time for which the deformity has been present as the same holds good for long-standing cases as well as the cases which developed the deformity very recently.

Summary.—In neural leprosy cases, even when they have developed drop foot and claw hand, the deep reflexes are exaggerated.

My thanks are due to the Superintendent, Government General Hospital, for permission to report this observation.

[The original manuscript was accompanied by a long table giving details of 24 cases and the deep reflexes present in them. This table has been omitted here in order to save space.

The observations recorded here are of interest. The author, however, is incorrect in saying that similar observations have not been recorded before.

The author's conception of leprosy appears to be that it causes a generalized peripheral neuritis, some nerves however showing more clinical

affection than others. If this conception of leprosy is true then some explanation of the retained reflexes in leprosy, such as is given by the author, is necessary. This conception of leprosy however is not that generally accepted, and leprosy is not generally regarded as a generalized peripheral neuritis. The presence of the deep reflexes in cases of neural leprosy is, we believe, due to the fact that usually in such cases only certain nerves, particularly more superficial nerves are affected, and these nerves happen not to be those which are concerned with the production of deep reflexes. For example, drop foot is caused by affection of the peroneal nerve which is not in any way concerned with the production of the ankle jerk. An observation that the ankle jerk is unaffected in leprosy foot drop is one we should expect. Similar remarks may be made about claw hand produced by involvement of the ulnar nerve which has no effect on the biceps and supinator jerks.—
EDITOR, I.M.G.]

SUB-TYPES OF CHOLERA VIBRIO ISOLATED FROM CHOLERA PATIENTS IN BOMBAY

By D. W. SOMAN

and

S. K. NAIL

(From Haffkine Institute, Bombay)

THAT the strains of cholera vibrio isolated in epidemic and sporadic outbreaks differed from each other on immunological grounds was first demonstrated by Japanese workers as early as 1913; they called them 'original' and 'varied' respectively (Kabeshmia, 1913). It was left to Gardner and Venkatraman (1935) however to confirm the existence of serological sub-types within the classical sub-group I among the diverse heat-stable O antigens, and to designate them as types 'Inaba' and 'Ogawa'.

Observations on the serological sub-types of cholera vibrio in relation to sporadic and epidemic outbreaks in different parts of India are very scanty. While a few such investigations undertaken refer to such areas as Northern India, Bengal, Assam, Burma and Madras, no information is available as to the serological sub-types encountered in outbreaks in and around Bombay. The object of this communication is, therefore, to record the results of such an investigation conducted during the recent outbreaks of cholera in Bombay City in the years 1943 and 1945.

Material for investigation was received from the isolation hospital in the city, and was dealt with as quickly as possible on arrival in this

laboratory. The failure or success of the isolation of any intestinal pathogen depends on a number of different factors, the selectivity of the medium being the most important. The value of DEC medium being definitely established as a very suitable and selective medium for the isolation of the common intestinal pathogens including the cholera vibrio (Soman, 1944), it was used during the past and present investigation. Altogether 37 strains of cholera vibrio were isolated during the 1943 outbreak, and 127 strains during the 1945 outbreak. They were all typical cholera vibrios, gave a positive cholera-red reaction and being non-hæmolytic (Greig's technique, 1914). They fermented saccharose and mannose with the formation of acid only, and did not ferment arabinose; thus they belonged to Heiberg's group I vibrios. They were agglutinated by cholera O serum group I, prepared in this Institute, and by that obtained from Kasauli. Their serological sub-types were further determined by slide agglutination tests with Inaba and Ogawa monospecific sera obtained from Kasauli, and also with the absorbed sera prepared at this Institute. Thirty-five out of 37 strains isolated in the 1943 outbreak belonged to the Ogawa sub-type, while two were found to be of Inaba sub-type. Inagglutinable vibrios were also isolated four times. Out of 127 strains isolated in the 1945 outbreak, 126 belonged to the Ogawa sub-type, and only one was found to be of Inaba sub-type. Inagglutinable vibrios were also isolated nine times. It is of interest to note that all Inaba strains were isolated only at the end of both the outbreaks. The Inaba strain isolated during the 1945 outbreak was found to be from an imported case from Bengal. The patient, a woman, came one month before to Malad, a suburb of Bombay, from her native place in Bengal. She gave a history that two days before she was attacked with vomiting and diarrhoea, and her servant had vomiting and diarrhoea, from which he recovered. The woman had to be admitted to the isolation hospital and was discharged after a few days.

During the present outbreak, 40 per cent of the positive isolations were made in cases coming from the neighbouring cholera-stricken districts, such as Nasik, Thana and Poona. One imported case was from Delhi. The serological sub-type determined for all these cases was Ogawa, and this was proved to be the prevalent sub-type during the years 1943 to 1945, not only in the City of Bombay but in the adjoining districts. No outbreaks of cholera in the city had been recorded in the annual reports of the Health Officer of Bombay Municipality since the year 1939 till the year 1943. Stray samples of stools from imported cases into the city or from district cases were received by this Institute for detection of vibrios, and the serological sub-types of these strains were

determined. The following is the record of such stray isolations:—

Year	Area	Sub-type and number of strains
1940	Ahmednagar	Ogawa 1
1941	Ahmedabad	Inaba 4
1943	Bombay	{ Ogawa 35 Inaba 2
1944	Nasik	Ogawa 2
1945	Bombay } Nasik } Thana } Poona }	{ Ogawa 926 Inaba 1

The production of monospecific Inaba and Ogawa sub-type sera made it possible to differentiate strains of the sub-type isolated from cholera cases in different parts of India. Inaba infections mostly prevailed over the greater part of Northern India, Bengal and Assam (Taylor, 1941). Strains isolated in Madras City and the northern districts of Madras Presidency in 1936 or before belonged to the Inaba sub-type, but those isolated from the southern part of the Madras Presidency were chiefly of the Ogawa type. From a severe epidemic in Madras district in South India, 84 strains isolated from cases belonged to the Ogawa sub-type (Venkatraman and Pandit, 1938). The observations and the study of two different sub-types in different parts of Madras Presidency did not reveal any epidemiological differences. Investigations carried out over a period of years in the Madras Presidency have shown extensions and recessions of the area in which the respective sub-types may be the form associated with outbreaks. A complete change also occurred in 1940, when the Ogawa sub-type was the form associated with an outbreak in the Northern Circars, all 252 strains being of this type (Taylor, *loc. cit.*). Similar changes were also observed in Bengal in 1938; 25 per cent of strains isolated in Calcutta were Ogawa (Pasricha, *et al.*, 1938).

In the absence of any previous record regarding the sub-types prevalent in the Bombay Presidency, the author felt it desirable to record the sub-types determined during the two recent outbreaks of cholera in the Bombay City, for future comparisons. The significance of serological sub-types need not be exaggerated, but such knowledge may be useful in tracing the source and following up the progress of an epidemic.

Summary and conclusions

The prevalent and predominant sub-types of cholera vibrio isolated during the outbreaks of 1943 and 1945, have been determined for the first time for Bombay City and the adjoining districts. One hundred and sixty-four strains isolated have been tested against cholera O serum group I and Inaba and Ogawa specific

sub-type sera. One hundred and sixty-one strains belonged to the Ogawa sub-type; the remaining three strains were found to be Inaba sub-type. No 'intermediate' type was recorded during the two outbreaks. Thus, the Ogawa sub-type infections were found to predominate during the recent outbreaks of cholera in this part of the country.

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A Mirror of Hospital Practice

IDIOPATHIC GANGRENE OF THE SCROTUM

By D. SHAMANNA

Assistant Surgeon, L. F. Hospital, Saklaspur (Mysore)

THE following case report might be of interest in view of Mair's article on 'Idiopathic gangrene of the scrotum' and the annotation on 'Regeneration of the scrotum' published in the *Lancet*, April 14, 1945.

A Muslim, aged 30 years, was admitted to the hospital for pain in the scrotum. He had noticed pain and a patch of redness in the scrotum on waking up one morning, and applied a poultice. Next day the patch sloughed out, leaving bare the corresponding area of the testes. The condition was growing rapidly worse and the patient came to the hospital on the third day.

On admission, the patient was dyspnoeic and restless and complained of intense pain in the scrotal region. Temperature 102°F., pulse 110 and respiration 25. Locally, except a little fringe at the base of the penis, the whole of the scrotum had sloughed out and was dangling *en masse* leaving both the testes bare. The discharge from the wound was extremely foetid. The inguinal glands on both sides were enlarged and threatening to suppurate. There was no difficulty in micturition and the other systems were normal.

Facilities for bacteriological examination of the pus not being available, the condition was treated on the assumption that it was gangrene of the scrotum. Removal of the slough, frequent irrigation of the wound with warm boric lotion, dressing it with cod-liver oil and sulphanilamide powder, and oral administration of sulphanilamide improved the general condition of the patient and checked the spread of infection. On the fourth day after admission, the patient was afebrile, pulse and respiration rates almost normal, pain considerably lessened and the swelling of the inguinal glands had subsided.

Surprisingly, with the continuance of this conservative treatment, the whole of the scrotum was reformed within five weeks.

MALARIAL INFECTION IN THE NEW-BORN

By R. N. VERMA

Resident Medical Officer, Shree Raghvendra Hospital, Bundi

I WAS called in to attend a baby 4 days old suffering from fever. The baby was very restless, with frequent retraction of legs on to the abdomen, and twisting of hands and arms.

The mother gave a history of fever 2 days before delivery, but the labour had been normal. The baby had been given a dram of castor oil, and there were 4 motions; it was also given 4 doses of a diaphoretic mixture on the previous day but with no improvement in the general condition.

On examination, the temperature was 103°F., the pulse too rapid to be counted, and the respiration hurried. A blood smear was taken at once and a large number of M.T. rings were found. The baby was put on mepacrine hydrochloride 1/16 mg. every 4 hours. Next morning the temperature came down to 99°F. but the general condition deteriorated and the baby died the same evening.

Clearly this was a case of congenital malaria, as M.T. rings were found in the blood 4 days after birth, and the incubation period of *P. falciparum* is 9 to 12 days. It is widely admitted that a healthy placenta will not permit malaria parasites to pass into the foetal circulation, but a damaged placenta will. On enquiry, I found that the placenta in this case was apparently healthy, and there was no history of injury either before or during labour. It seems possible that malarial infection may set up certain pathological changes such as hyperplasia in the placenta, under which conditions malaria parasites may pass from the mother's to the foetal circulation.

PAPILLOMA OF THE BLADDER IN A CHILD THREE YEARS OLD

By GHULAM NABHI, L.M.P.

A HINDU male child, three years old, was admitted to hospital with difficulty in passing urine, and distension of the bladder. The symptoms were of two months' duration. The passage of a sound failed to detect the vesical stone. X-ray examination revealed no stone. Symptomatic treatment gave no relief. Suprapubic cystotomy was performed, and a soft growth about one inch long was found arising from the margin of the internal urethral orifice. The bladder was closed and a self-retaining catheter was left in place. Recovery was uneventful.

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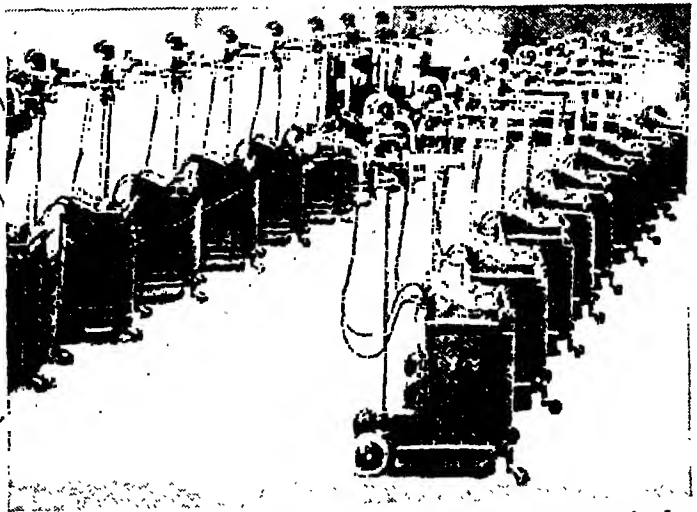
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Indian Medical Gazette

OCTOBER

BERI-BERI: ADULT AND INFANTILE

BERI-BERI is a disease which is found to be common most when polished rice forms the bulk of the diet. It is endemic in Japan, South China, the Philippines, Siam and the Malay Peninsula and other areas, and is a very important cause of morbidity and mortality. It is reported as a common cause of infant mortality in Japan, and before the war was reported as one of the commonest sources of sickness in the Japanese army. The editor remembers seeing large numbers of cases of beri-beri in North Siam about 15 years ago and also in the Chinese in various parts of the East. In most parts of India, however, the fully developed syndrome of peripheral neuritis frequently with cardiac affection and attributed to vitamin deficiency is rare. It has been stated, however, that vitamin-B₁ deficiency is very common in pregnant women in South India although typical cases of beri-beri are not common either in India or in South India as a whole. There is, however, one part of South India where beri-beri is not uncommon, viz the Northern Circars area of the Madras Presidency. The reason for the rareness of typical beri-beri in many parts of India is not fully understood. The use of rice parboiled before milling in many areas (but not in the Northern Circars) is said to be the main factor.

The whole question of the ætiology of beri-beri has been a subject of much discussion. On this subject Bicknell and Prescott state as follows:

'It has been generally supposed that beri-beri is a deficiency disease due to lack of vitamin B₁. Deficiency diseases, however, are never limited to lack of a single factor, and although there is a vitamin-B₁ deficiency in beri-beri, the disease is undoubtedly an avitaminosis due to lack of the whole of the B group. Because the oedema and cardiovascular symptoms of beri-beri respond dramatically to pure vitamin B₁ it has been argued that beri-beri is therefore a disease specifically associated with a deficiency of this vitamin. It is possible that in beri-beri the graver signs and symptoms of vitamin-B₁ deficiency, which are neurological and cardiovascular, manifest themselves before those of other B complex deficiencies. When pure synthetic vitamin B₁ became available it was found to produce a rapid cure of certain manifestations of beri-beri, but some persisted or even grew worse. It is now recognized that the treatment of beri-beri is more satisfactory with vitamin B₁ and foods or concentrates rich in the B complex than with pure vitamin-B₁ alone. Recent observations on induced vitamin-B₁ deficiency have also shown that it is impossible to produce beri-beri experimentally in many people by diets poor in vitamin B₁ only. Local custom and food habits determine whether an endemic vitamin-B deficiency manifests itself as beri-beri, pellagra or ariboflavinosis. No selected combination

of foods is entirely lacking in one vitamin. Clinically, few patients present all the classical signs attributed to any avitaminosis; actually any one case if carefully examined shows those of several. Certain manifestations are common to beri-beri and pellagra, e.g. weakness, nervous irritability, vague malaise, lassitude, mental confusion, depression and inability to concentrate. Beri-beri patients often show the skin lesions or the glossitis of nicotinic acid deficiency and the cheilosis of ariboflavinosis.'

Bicknell and Prescott go on to quote various workers who have questioned the view that vitamin B₁ is the specific anti-neuritic vitamin.

Adult beri-beri has been known for many centuries in Japan and has been the subject of special study by numerous workers, Japanese and others during the last 50 years. It was a Japanese worker who 50 years ago first described infantile beri-beri differing in many important points from the adult type of beri-beri. It appears in the first three months of life in children who are breast fed, and it is characterized by rapid onset, rigidity of the body, fretfulness, constipation, oedema of the extremities, low urine output, enlargement of the heart, tachycardia, and cyanosis and sometimes sudden death. Early symptoms are described as vomiting, anorexia, diarrhoea with green stools. The infant is often attacked with sudden paroxysms of pain causing tenderness and rigidity but not true convulsions. Aphonia is common and is said to be characteristic, and the beri-beri cry is said to be diagnostic. Laryngoscopy may show cord paralysis. The pulse is feeble and rapid, the neck veins are prominent and the face cyanosed. Death can occur within a day or two unless vitamin B₁ is given.

Many years ago the acuteness and severity of infantile beri-beri was recognized, and it was considered that although the disease appeared in breast-fed children of mothers showing signs of beri-beri, the ætiology of infantile beri-beri was possibly or probably different from that of adult beri-beri. According to Fehily the term 'breast milk intoxication' was suggested by Ito in 1911, and Fehily states that recent investigations of infantile beri-beri have simply confirmed the idea that it is an intoxication and not the direct result of an avitaminosis. Fehily has surveyed the matter in a number of papers published in recent years, on the basis of a special study of the disease in maternal and child welfare centres in Hong Kong. Numerous workers have shown that in the absence of vitamin B₁, the oxidation of carbohydrates to their end products is incomplete, and they accumulate as intermediate metabolites which have been shown to be toxic. One toxic substance, methyl glyoxal, has been shown to be present in considerable amount in human beings with avitaminosis, and in the milk of avitaminotic mothers, and it is suggested that it is the presence of this group of toxic substances in the human milk that causes infantile beri-beri. These facts are quoted to explain how infantile

beri-beri can appear so very quickly even after a few breast feeds. It is true that the children of avitaminotic mothers have a very low vitamin-B intake, but they rarely show signs of beri-beri as seen in the adult. It is postulated that they suddenly develop 'milk poisoning' when any vitamin B they have in the body is exhausted and with the increase in the toxic property of the mother's milk. It is stated however that the post-mortem findings in infantile beri-beri are similar to, but less marked and less constant than, those seen in adult beri-beri.

Fehily, in a recent article, discusses at length the diagnosis of infantile beri-beri and the difficulty of detecting the condition in a child who is often over-weight and shows no physical sign of disease, the symptoms being mainly vomiting after meals. She stresses the importance of this vomiting after meals of the fat, pale, flabby child with enlargement of the heart and some sign of cyanosis and dyspnoea. Loss of voice and the bringing up of mucus in the throat in a peevish, restless child who cries a lot sometimes arouses the suspicion of infantile beri-beri. Some bronchitis and slight fever may be present. The hoarseness may be wrongly attributed to laryngitis. Fehily stresses the characteristic aphonia and the visible but inaudible cry of the child. She attributes this to oedema of the mucous membrane and mucus collection in the throat, and oedema of the respiratory tract. Fehily discusses the differential diagnosis of the condition in children from dyspepsia, with flatulence (which is a common sign in infantile beri-beri), meningitis, nephritis, peritonitis, helminth infection, tetany, etc., and from broncho-pneumonia, bronchitis, laryngismus stridulus and other similar conditions. She also describes chronic infantile beri-beri and deals with its differentiation from other forms of malnutrition, and since all these may be co-existent, differentiation is often difficult. It is noteworthy that acute oedema is not characteristic of infantile beri-beri either in its acute or chronic forms, and if oedema is present, it is often localized.

Since in the Northern Circars, at any rate, adult beri-beri is by no means rare, it was presumed that infantile beri-beri would also occur, although its occurrence in India has, as far as we know, only recently been recorded. In our present issue we publish an article on infantile beri-beri by Krishnan, Ramachandran and Kamala Sadhu, although the authors do not like the use of this term and avoid it in the paper. Nevertheless, it is obviously this condition which they are describing. We think it more than possible that this condition would be found in other areas of India, even in areas where adult beri-beri in its typical forms are not seen. In other countries it is frequently found that the mother, although showing signs of vitamin-B deficiency, need not show the classical picture of beri-beri for actual infantile

beri-beri to be seen in the baby she is breast feeding. We therefore think that this discussion of infantile beri-beri contained in this issue may be of some general interest, and might enable the condition to be more widely recognized in India.

J. L.

THE INTERVERTEBRAL DISC AND SCIATICA

THE aetiology of the conditions of sciatica and low back pain have long been the subject of discussion in medical literature, and widely divergent views on the aetiology have been expressed by different workers. In recent years, however, numerous articles have appeared expressing the opinion that sciatica is often, though not always, caused by disease of the intervertebral discs in the lumbar region. A similar aetiology has been postulated for low back pain with or without sciatica. While these ideas have been hotly contested by certain writers, there seems to be a definite swing of opinion in support of these ideas.

This swing of opinion is reflected in an article in the *Medical Journal of Australia*, August 1945, p. 244, by James H. Young. This article starts with the following two sentences :

'My ideas on the subject of low back pain are now radically different from those expressed in a paper published two years ago. At that time I held orthodox views—views which were, of course, never based upon any proved physiological or pathological findings.'

The second sentence is an amazing one to find in a scientific paper in a scientific journal. If the views were not based on proved physiological or pathological findings why were they ever published? The phrase 'of course' would imply that this is a not uncommon procedure in medical literature. Is this really so? The frankness of the above two sentences, however, is refreshing. We find a similar frankness in some of the recent medical publications, authors frankly admitting in print the mistaken nature of the views and judgments previously expressed by them. This is a very healthy tendency seen in some recent medical literature. The good physician or surgeon is not the man who never makes mistakes, but is the man who when he does make a mistake recognizes it as such, acknowledges it to himself and to other medical men, and above all learns from his mistakes.

To return however to the subject of the intervertebral disc, the present tendency of opinion is well reflected in the summary of the article above referred to which includes the following sentences :

'The lumbar intervertebral discs are a major factor in the production of low back pain. Root pains are not necessary either for diagnosis or for localization.'

beri-beri can appear so very quickly even after a few breast feeds. It is true that the children of avitaminotic mothers have a very low vitamin-B intake, but they rarely show signs of beri-beri as seen in the adult. It is postulated that they suddenly develop 'milk poisoning' when any vitamin B they have in the body is exhausted and with the increase in the toxic property of the mother's milk. It is stated however that the post-mortem findings in infantile beri-beri are similar to, but less marked and less constant than, those seen in adult beri-beri.

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The cervical intervertebral discs are often the site of pathological processes. The resulting symptoms include stiff neck, shoulder girdle pain and cervicobrachial pain. These have hitherto been labelled fibrositis, brachial neuritis and spondylitis. Future progress in this field will continue to be extensive, and must include careful clinical and radiological examination of patients such as I have indicated.

In the intervertebral disc lies the key to a large part of the problem of so-called rheumatic disorders.'

It must however not be thought that here lies an easy solution to all the sciatica and low back pain. The following paragraph on the subject of sciatica is quoted from the publication on Medical Progress, 1943, of the *British Encyclopædia of Medical Practice*, p. 4:

'This common and crippling complaint still challenges medicine to produce an explanation of its mechanism and to find a rational and effective treatment. The ruptured intervertebral disc has become a popular explanation as a causative lesion, but it is not clear why it should cause an intermittent and not a continuous sciatica, nor is operative removal of the excrescence an unqualified success. J. H. Kellgren's work (1941) on the reference of pain from one area to another within the territory of deep tissues supplied by one spinal segment gives precision to the idea of referred sciatic pain due to lesions of joints, ligaments and fibrous tissues in the lumbar and sacral regions, and encourages the search for such lesions and their infiltration with a local anæsthetic. Text-book sciatic neuritis, if such exists, is taking a back seat among the causes of sciatica. But much observation and study are yet required to put the management of cases of sciatic pain on a satisfactory basis.'

J. L.

PALUDRINE—M.4888

RECENTLY, the news from England and the daily press in England have included items regarding the new potent anti-malarial drug named 'Paludrine' (or M.4888) of the Imperial Chemical (Pharmaceuticals) Ltd., Manchester. No detailed medical reports are available on this preparation. It is believed that the drug has been thoroughly tested in cases of malaria in England and particularly at the Liverpool School of Tropical Medicine. It is apparently claimed that the new drug is much more effective than quinine and the previously available synthetic anti-malarials. This is good news indeed and we hope soon to have some of the drug to try in malaria in India. There is every reason to believe that an important new discovery has been made.

It is a little unfortunate that the same name 'Paludrine' was applied to a previous product of the same company for a drug which bore the number M.3349 and which was designed for the

treatment of malaria. Possibly the only published account of the use of this drug in human malaria was made in the *Indian Medical Gazette*, May 1945, by Das Gupta, Lowe and Chakravarty, who found that the drug, while effective in malaria, appeared to be toxic in certain cases to such an extent as to preclude its general use in malaria. This is apparently accepted by the manufacturers, who have now introduced this newer drug M.4888 which is said to be vastly superior to the previous one. The manufacturers are now applying the name 'Paludrine' to this new drug, the old drug apparently being no longer prepared or used. A letter from the manufacturers on this subject is published in our correspondence columns in this issue. We wish to make this position clear to our readers, since paludrine will apparently play an important part in the treatment of malaria in future, and since publications on it are likely to be numerous. In this journal, apparently the only journal in which the name paludrine was used for the old drug, the name paludrine will in future be used for the new drug. If need arises to refer to the old drug, it will be called M.3349.

We hope that the manufacturers realize fully that any drug which aims at being widely used in India for malaria must be cheap, and we hope that steps will be taken to put this new drug on the market at a price which will make it possible for the millions of patients with malaria in India to use it. This means not only a low price, but a very low price, because of the poverty of most people in this country. A copy of this note is being sent to the manufacturers.

J. L.

Medical News

THE INDIAN HONOURS LIST

14TH JUNE, 1945

THE following are the names of medical men, and others associated with medical institutions, in the Indian Honours List of date 14th June, 1945. We offer them our congratulations.

C.I.E.

Lieutenant-Colonel K. R. K. Iyengar, O.B.E., I.M.S. (Retired), Director, Pasteur Institute of Southern India, Coonoor, Madras.

O.B.E.

Lieutenant-Colonel A. N. Chopra, I.M.S., Inspector-General of Prisons, and Director of Health, Orissa.

Lieutenant-Colonel M. Sendak, I.M.S., Superintendent, Special Prison, Ahmednagar Fort, Bombay.

J. S. Tilley, Esq., Deputy Red Cross Commissioner, War Supplies Depot, Bombay.

M.B.E.

Miss Dev Priya Bali, W.M.S., Deputy Inspector-General of Civil Hospitals (Women), United Provinces.

Miss Hope Lucas, Nursing Superintendent, Bowring and Lady Curzon Hospitals, Bangalore.

P. K. Biswas, Esq., Civil Assistant Surgeon, Bengal.

S. Ghosh, Esq., Professor of Chemistry and Physics, School of Tropical Medicine, Calcutta.

Kaisar-i-Hind Gold Medal

Miss Jessie Findlay, Principal and Professor of Surgery, Women's Medical College, Vellore, Madras.
B. L. Carruthers, Esq., Director, Medical Centre, Miraj.

Kaisar-i-Hind Silver Medal

Lady Doris Birkmyre, Honorary Regional Staff Officer (Welfare), Indian Red Cross and St. John Joint War Organization, Calcutta.

Miss Jean Arthur Gemmell, w.m.s., Medical Superintendent, Alice Horsman Memorial Hospital, Cawnpore, United Provinces.

Mrs. Lilian Gertrude Holder, Vice-President, Shillong Red Cross Committee, Assam.

Miss Edith Marv Mann, Nursing Superintendent, Chittagong General Hospital, Bengal.

Miss Wilhelmina Noordyk, Nursing Superintendent, Seudder Memorial Hospital, Ranipet, Madras.

Mrs. Perin Darashaw Vakharia, Honorary Treasurer, Ladies Red Cross Work Party, Broach, Bombay.

Miss Annie Elizabeth Young, Nursing Superintendent, Lady Willingdon Hospital, Lahore, Punjab.

Miss Bessie Young, Matron, Government Tuberculosis Sanatorium, Dadar, North-West Frontier Province.

G. S. Evite, Esq., Medical Superintendent, Sir William Wanless Tuberculosis Sanatorium, Wanlesswadi, Bombay.

The Reverend F. R. Lazarus, Honorary Superintendent, Cuttack Leper Asylum, Orissa.

Bar to the Kaisar-i-Hind Silver Medal

Miss Jennv Gauld, Lady Minto's Indian Nursing Association, Delhi.

Kaisar-i-Hind Bronze Medal

Mrs. Josephine Ernestina Benjamin, Lady Doctor, Municipal Zenana Hospital, Bannu, North-West Frontier Province.

Mrs. Vasundhara Vinayak Gharpure, Lady Doctor-in-charge, Indian Troops Families Hospital, Royal Bombay S. and M. Group, I.E., Kirkee.

Mrs. Lucy Richardson, Sister, Medical College Hospitals, Calcutta.

M. X. de Noronha, Esq., Honorary Radiologist, Ursula Horsman Memorial Hospital, Cawnpore, United Provinces.

Khan Jahan Khan, Doctor-in-charge, Mission Hospital, Karak, North-West Frontier Province.

T. Kuki, Esq., Doctor-in-charge, Manipur State Hospital, Ukhrul, Assam.

Khan Bahadur

Syed Niamathulla, Private Medical Practitioner, and Ex-Mayor, Corporation of Madras.

Khan Sahib Syed Tajuddin Sahib Bahadur, Private Medical Practitioner, and President, The Hood Co-operative Institute, Tanjore, Madras.

Khan Sahib C. M. Ahmad, Hospital Surgeon, Punjab Veterinary College, Lahore, Punjab.

Rai Bahadur

P. N. Sen, Esq., Civil Surgeon, Jaunpur, United Provinces.

R. M. Das, Esq., Santi and Kamini Tea Estate, Hoogrijan, Lakhimpur, Assam.

Rao Bahadur

R. M. Mathew, Esq., Assistant Director of Public Health, Madras.

M. S. Kripalini, Esq., Medical Practitioner, Hyderabad, Sind.

Khan Sahib

M. M. Hossain, Esq., Medical Practitioner, Bagerhat, Khulna, Bengal.

A. A. Khan, Esq., Medical Officer-in-charge, Colvin Hospital, Allahabad, United Provinces.

M. A. Alvi, Esq., District Medical Officer of Health, Moradabad, United Provinces.

R. Hussain, Esq., Assistant to the Civil Surgeon of Patna, Medical Officer-in-charge, Patna Police Hospital and Lecturer in Medical Jurisprudence, Patna Medical College, Bihar.

S. M. A. Rahman, Esq., Civil Surgeon (officiating), Bilaspur, Central Provinces and Berar.

Rai Sahib

J. Banerjee, Esq., Civil Surgeon, Khulna, Bengal.

B. N. Mukharji, Esq., Medical Officer, His Excellency the Governor's Staff Dispensary, Bengal.

T. S. Shukla, Esq., Civil Surgeon (officiating), Ghazipur, United Provinces.

R. N. Tandon, Esq., Medical Officer-in-charge, Sadr Hospital, Gorakhpur, United Provinces.

B. B. Mukharji, Esq., Assistant Surgeon, Gaya Pilgrim Hospital, Gaya, Bihar.

Y. Sinha, Esq., Homoeopath, Laheriasarai, Darbhanga, Bihar.

Rao Sahib

R. V. P. C. Pillai, Esq., Private Medical Practitioner, Tinnevely, Madras.

N. Krishnaswami, Esq., Senior Sub-Assistant Surgeon, Bowring Civil Hospital, Bangalore.

O.B.I.

To the First Class with the title of 'Sardar Bahadur'
Indian Army Medical Corps

Subedar-Major Muhammad Ismail, Bahadur, O.B.I.

Subedar Sunder Singh, Bahadur, O.B.I.

Subedar-Major Muhammad Shafia, Bahadur, O.B.I.

Subedar-Major Babu Singh, Bahadur, O.B.I.

Subedar-Major Amar Nath Chopra, Bahadur, O.B.I.

Subedar-Major Kartar Singh Bewal, Bahadur, O.B.I.

Subedar-Major Arjun Singh Dhillon, Bahadur, O.B.I.

Subedar-Major Hardyal Singh, Bahadur, O.B.I.

Subedar-Major Arjun Singh Sekhon, Bahadur, O.B.I.

Subedar Bishan Das Minocha, Bahadur, O.B.I.

Subedar-Major Hirde Narain, Bahadur, O.B.I.

Subedar-Major Udhram Singh, Bahadur, O.B.I.

Subedar Daval Singh, Bahadur, O.B.I.

Subedar Balwant Singh, Bahadur, O.B.I.

Subedar-Major Rajindar Singh, Bahadur, O.B.I.

Subedar-Major Atma Ram, Bahadur, O.B.I.

To the Second Class with the title of 'Bahadur'

Subedar-Major Haqiqat Rai.

Subedar Kundan Lal Jaini.

Subedar-Major Palathunkal Ipe Ipe.

Subedar-Major Pitam.

Subedar-Major Gazi Ram.

Subedar Muhammad Wasil Khan.

Subedar Balwant Rai Puri.

VITAMIN A REQUIREMENTS. EXPERIMENTS IN BRITAIN*

IN response to a request from the Ministry of Food, the Vitamin A Sub-Committee of the Accessory Food Factors Committee (Lister Institute and Medical Research Council) undertook an experiment to obtain information on the human requirement of vitamin A and of carotene. The experiment was carried out at the Sorby Research Institute, Sheffield, for the Medical Research Council, by which it was financed. It lasted from July 1942 until October 1944.

Twenty-three 'conscientious objectors', twenty men and three women, volunteered to live on a diet designed to be deficient in these substances but complete in every other respect. The absence of vitamin A and its precursors was confirmed spectrophotometrically and biologically. Young rats fed on the diet grew well when supplied with vitamin A but, without it, failed to thrive and their livers at autopsy were devoid of vitamin A. The disappearance of carotene from the

* Abstracted from *Features* pamphlet, No. 198, dated 21st September, 1945, of the Bureau of Public Information, Government of India.

blood plasma of the deprived volunteers confirmed the absence of these substances from the diet. Prophylactic therapeutic tests were made with vitamin A and carotene, and faecal excretion tests were made with carotene from different sources. No attempt was made to differentiate between the biological values of different isomers of carotene.

As the experiment lasted more than two years, the results obtained were extensive and cannot quickly be prepared for publication, but, since their implications in assessing nutritional status and requirements in respect of vitamin A are far-reaching, the chief conclusions about which the team of workers is unanimously in agreement are given below.

With efficiency for dark adaptation and plasma values for vitamin A as criteria, none of the sixteen deprived subjects became depleted within a year. Eleven of these continued the test for more than thirteen months, and only three showed marked signs of depletion after fourteen, seventeen and twenty-two months, respectively. Most of the remainder showed no changes attributable to vitamin-A deficiency, except a gradual fall in the plasma value for vitamin A, estimated by the antimony trichloride method; but one failed to show this sign of deterioration even after twenty-two months. The state of the vitamin-A reserves of this sample of the population of Great Britain in the summer of 1942 would thus seem to have been sufficient to meet the requirements for from one to two years. This conclusion is in harmony with the finding, at about the same period, of a median value of 600,000 I.U. for the total vitamin-A reserves of the liver, determined at autopsy, in cases of accidental death.

In the three markedly depleted subjects, the value for vitamin A in the blood plasma declined from about 90 I.U. per 100 ml. to about 30 I.U. In the test of the capacity for dark adaptation, measured with the Wald-Steven modification of the Hecht-Shlaer adaptometer, the values for the final rod-threshold ranged, at the start, from 1.55 to 1.95 log. micromillilamberts, and rose to between 2.38 and 3.44; at about the same time, the time of transition from cone to rod vision, which was at first from five to ten minutes, increased to as much in one case as thirty-three minutes.

In contrast with the slow fall in the value for vitamin A in the plasma which occurred in almost all the subjects undergoing depletion, the value for total carotenoids fell quickly and remained low. Chromatography of a pooled sample of plasma after nine months of depletion showed it to contain 18 μ gm. total carotenoids per 100 ml., but no measurable amount of A- or B-carotene. The value for the final rod-threshold in all the subjects, whether undergoing depletion or not, deteriorated significantly during the first winter, seven months from the start, but, in most cases, recovered in the spring to the initial level. The explanation of this phenomenon is unknown, but the risk of misinterpretation thus introduced is clearly great.

The value did not again deteriorate significantly until much later, when the plasma value for vitamin A had declined to about 40 I.U. per 100 ml. There did not appear to be any correlation between the value for vitamin A in the plasma and the value for the final rod-threshold until both had deteriorated significantly.

Three different laboratories carried out the blood tests, the samples being distributed by post; their results often varied much for the same sample, but the average of a sufficient number yielded consistent results. All three laboratories agreed that no great reliance could be placed on the result of a single estimation for vitamin A in plasma.

From the thirteenth month of the experiment onwards, P. C. Livingstone applied his new technique of rod scotometry to examination of the volunteers. By this method the field of vision was mapped under conditions of dark adaptation with test objects of known very low luminosity. The technique confirmed the existence of defective night vision in the three volunteers whose final rod-threshold was raised and

cone-rod transition time lengthened. In addition, this method revealed the night vision as defective in five of the other deprived subjects who gave normal readings with the adaptometers of Craik and of Wald and Steven. On treatment with vitamin A or carotene, the scotometry readings returned to normal. Rod scotometry thus seemed to detect deterioration of capacity for dark adaptation earlier than was possible by measurement of the dark-adaptation curve.

There were no objective changes on general clinical examination, or conjunctival changes perceptible with the slit-lamp microscope; there were no changes in the blood picture or platelet count. Only one subject showed follicular hyperkeratosis, but a study of the case history indicated that the condition was present from the start and was not specifically affected by variations in the vitamin-A supply. There were no definite changes in response to memory and fatigue tests. There was no consistent loss of weight.

A comparison of the dietary and faecal carotene for the volunteers receiving a carotene supplement showed that the disappearance of carotene from the gastrointestinal tract was highest when the carotene was dissolved in fat (arachis oil or margarine); on the average, 28 per cent of carotene given in this form was excreted. The percentage excretion of carotene from green vegetables (cabbage or spinach) was in the region of 60, and from sliced carrots in the region of 75. The individual variations were wide.

Seven volunteers without previous depletion received, for periods of from six and a half to twenty-two and a half months, a daily supplement of about 2,500 I.U. vitamin A as distilled natural esters in oil, or of about 5,000 I.U. carotene, in oil or from various natural sources, and showed no changes attributable to vitamin-A deficiency.

The three subjects who developed defective night vision and low plasma values for vitamin A were dosed with vitamin A- or B-carotene in oil while the deficient diet continued. In one case treatment with a daily dose of 1,300 I.U. restored dark adaptation and plasma vitamin-A values to normal levels within five months. A second case did not respond to a dose of 1,300 I.U. carotene daily but improved in the course of five months when the dose was changed to one of 2,600 I.U. daily. In the third case, where the degree of deficiency was milder, a daily dose of 2,600 I.U. carotene promptly improved dark adaptation and the concentration of vitamin A in the plasma.

When the amount of carotene excreted was deducted, the amount of vitamin A and of carotene which brought about the same result would thus appear to be about the same.

For assessing the requirement the relevant results are the following:—

A daily dose of 1,300 I.U. vitamin A or of 2,600 I.U. carotene was sufficient to cure a mild state of vitamin-A deficiency. The body reserves of vitamin A, presumed as already mentioned to have had a median value of about 600,000 I.U., were sufficient in all sixteen deprived subjects to prevent the onset of definite signs of vitamin-A deficiency for from twelve to twenty months; such a reserve would correspond with an average rate of consumption of 1,300 I.U. daily for fifteen months.

Thus, inclusion in the diet of a daily dose of 2,500 I.U. vitamin A, or of 5,000 I.U. carotene, may be regarded as adequate for maintenance of normal human adults and as leaving a fair margin of safety.

MONTHLY CLINICAL MEETINGS AT THE SCHOOL OF TROPICAL MEDICINE, CALCUTTA

MONTHLY clinical meetings at 4-30 p.m. on the first Wednesday in each month have been inaugurated. At the first meeting held on the 3rd October, 1945, there was a large attendance of civil and military medical men and women. The following cases were shown and discussed.

Dr. Galstaun showed four cases of osteopoikilia. Three of these were of the classical Albers-Schönberg

type. The unusual finding of a marked increase in the serum calcium was reported in two of these cases. The fourth case was of the rare type described by Voorhoeve where the stippling is replaced by parallel or radiating plaques. In this case the serum calcium was normal. All the cases were examined as the result of injury (? fracture), and none of the cases showed any clinical sign other than that of injury.

Captain Somerset showed a case of xeroderma pigmentosa (Kaposi's disease) in a female aged 16, with pigmentation of the skin and corneal ulceration in both eyes. The skin showed small areas of hyperpigmentation and hypertrophy, most marked on the face.

Dr. Ukil showed a case of bronchiectasis in a female child, probably developed from an unresolved pneumonia at the age of 5. A feature of the case was the presence of 'friction râles' audible over all the zones of the right lung. The not infrequent occurrence of bronchiectasis in India was stressed and the aetiology, pathogenesis, diagnosis, prognosis and treatment were outlined. The importance of lipiodol bronchography in diagnosis was stressed.

Dr. Lowe showed a case of acute infantile hemiplegia in a child aged 3 years. The child was admitted to hospital with chronic malaria, dysentery and hypoproteinaemia, and while in hospital developed the condition, a complete hemiplegia of the whole of the left side of the body. The suggested diagnosis was acute cerebral palsy of childhood. The alternative diagnoses of acute miliary tuberculosis, pyæmic abscess, cerebral malaria, in this case were discussed, but considered unlikely.

Dr. Lowe also showed a case of Parkinsonism following a febrile attack, probably acute encephalitis.

Dr. L. M. Ghosh showed a case of multiple and widespread liomyomata of the skin and discussed the diagnosis of the condition, its differentiation from Von Recklinghausen's disease, etc.

Dr. P. C. Sen Gupta showed a case of kala-azar complicated by cancrum oris involving the soft and hard palate on one side and described the striking results of penicillin in the treatment of this case. The acute process stopped immediately, the lesion quickly became quite clean, and shortly afterwards the dead bone separated spontaneously and the lesion healed.

Dr. Dharmendra showed two cases of leprosy, one of neural type with a patch on the forearm and thickening of most of the cutaneous nerves and nerve trunks of the arm; and one of lepromatous type in which there was involvement of the whole skin of the body with very little in the way of visible lesions. The skin and mucous membrane, however, showed large numbers of bacilli.

DEPARTMENT OF FOOD, GOVERNMENT OF INDIA, NEW DELHI. BULLETIN NO. 7, 'NUTRITION', JULY 1945

This bulletin, like its predecessors, will be a very interesting and useful one to the laity in this country. Its 20 pages contain authentic information under the following headings: the economics of diet; chart showing comparative vitamin 'A' and 'C' contents of rice, wheat and fruits; the campaign for better food; nutrition work in the provinces; radio questions and answers; more experiments at Coonoor; food facts; food flashes; the problem of milk; separated milk powder; on the kitchen front—recipes; Bangalore subsidizes milk for its children; nutrition research.

MEDICAL RESEARCH COUNCIL WAR MEMORANDUM NO. 14. NUTRITIVE VALUES OF WARTIME FOODS. HIS MAJESTY'S STATIONERY OFFICE, LONDON. Pp. 59. PRICE, 1s. 0d. 1945.

THE differences between the values for the composition of wartime and peacetime foods are often great

and this memorandum has been prepared to meet the demand of the dietary surveys of the population which are being carried out by the Ministry of Food and the Ministry of Health. For raw foods, the values for proteins, fats, carbohydrates and for the relatively small number of minerals and vitamins most likely to be deficient in human diet, are compiled from the results of direct analyses carried out in Britain and from the literature, and are given in 3 tables. These tables are suitable for evaluating dietary surveys and may also be found convenient in planning human dietaries where a high degree of scientific accuracy is not required.

SULFADIAZINE IN TREATMENT OF RELAPSE-ING MALARIAL INFECTION DUE TO PLASMODIUM VIVAX

THIRTY-THREE patients with vivax malaria acquired in the South-West Pacific area were treated with sulfadiazine over a two-week period. Acute clinical symptoms were controlled by a course of atabrine or quinine immediately preceding sulfadiazine therapy. Sulfadiazine blood levels of 4.7 to 10.7 mg. per hundred cubic centimetres were obtained in each instance. Follow-up on these patients three months later revealed that 16 had relapses, an incidence of 48.5 per cent, whereas our relapse rate for patients treated by usual courses of atabrine or quinine was 46.7 per cent.

Sulfadiazine is of no value in preventing relapses in the strain of *P. vivax* malaria naturally acquired in the South-West Pacific area and deserves no place in the therapy of this type of malaria.

(Abstracted from the *Journal of the American Medical Association*, 5th May, 1945.)

UNITED PROVINCES MEDICAL COUNCIL

At the meeting of the United Provinces Medical Council held at Lucknow on the 22nd and 23rd March, 1945, the following resolution was referred to the standing committee for careful consideration and redrafting:

'This Council recommends to the Provincial Government and through it to the Government of India that the practice of quackery is increasing daily in the country and as the Indian (Medical) Degrees Act (Act VII of 1916) and United Provinces Medical Registration Act (Act III of 1917) have failed in their purpose of protecting the practice of scientific medicine, the necessary legislation on the following lines be undertaken as early as possible:

- (i) It should be a penal offence to use the prefix "Doctor" or "Dr." by any one unless he possesses either a degree of doctorate from a recognized university or a medical qualification registrable by the Indian Medical Council or one of the Provincial Medical Councils or both.
- (ii) It should be a penal offence to use suffixes and/or prefixes simulating recognized medical degrees or diplomas.
- (iii) It should be a penal offence for anyone to practise scientific system of medicine (Allopathy) unless he holds a medical qualification registrable by either the Medical Council of India or by any one of the Provincial Councils or both.'

I. A. M. C. JOURNAL, VOL. 1, NO. 2

THIS second number of this new journal contains several items of interest to service medical men and also five articles giving up-to-date summaries of the present knowledge on the important diseases such as anæmia, kala-azar, hepatitis, sciatica, etc., by eminent military medical authorities.

Public Health Section

THE TREATMENT AND PREVENTION OF VITAMIN-B₁ DEFICIENCY IN INFANTS: A PUBLIC HEALTH EXPERIMENT

By RAO SAHIB B. G. KRISHNAN

Assistant to the Director, Nutrition Research Laboratories, Coonoor

S. RAMACHANDRAN

Municipal Health Officer, Cocanada

and

KAMALA SADHU

Additional Municipal Health Officer, Cocanada

AYKROYD AND KRISHNAN (1941) reported cases of infantile beri-beri in the Northern Circars area in the Madras Presidency, where beri-beri in adults was known to be common*. They found that in three towns, Bezvada, Cocanada and Vizagapatam, a peak in infant mortality occurred at the fourth month of life, while this peak was absent in other towns outside the beri-beri area. They concluded that infantile beri-beri was the chief cause of the unusual infant mortality. No direct clinical evidence was, however, available as to the prevalence of the disease, nor had any systematic attempts at prevention or treatment been made. To follow up the preliminary investigations, an 'infantile beri-beri enquiry' was undertaken in 1942 in Cocanada under the auspices of the Indian Research Fund Association. With the co-operation of the municipal authorities, the municipal health officer and the director of public health, Madras, one of the municipal infant welfare centres in Cocanada was taken over for purposes of the enquiry, and this was placed in charge of a lady health officer.

The present paper gives an account of the work of the centre. It confirms the provisional conclusion that infantile beri-beri is common in this part of India and indicates ways and means of attacking an important public health problem by the use of preparations of synthetic vitamin B₁.

Clinical

'Infantile beri-beri' is not a satisfactory name for the condition in infants with which

this paper deals. This condition does not, in its symptomatology, closely resemble adult beri-beri in its classical forms. Since it responds dramatically to treatment with pure vitamin B₁, and appears to be closer to an unmixed single vitamin deficiency than any other condition reported in human beings, it could reasonably be called 'vitamin-B₁ (or thiamin) deficiency in infants'. This is, however, a clumsy title. The population of the Northern Circars has coined a word—'anasa'—which is used to describe the disease, but, while most 'anasa' is vitamin-B₁ deficiency, the same name is also applied to other forms of disease in infants. Hence 'anasa' is scarcely appropriate as a scientific medical term.

The following clinical account of the condition was given by Aykroyd (1943):

'Infantile beri-beri occurs in breast-fed infants usually from the second to the fifth month of life. In the acute form, known to the Chinese as "Fung-Team" or "wind-mucus", the infant may suddenly become cyanosed, with dyspnoea and tachycardia, and die in a few hours. The disease may show itself in an infant in apparent health with few premonitory signs. Because of their acute fulminating nature, such cases may rarely be seen by the physician or welfare worker, but mothers with infants showing the condition in less desperate form may give a history of the sudden death in this fashion of other infants in early infancy. In Singapore (Faris, *loc. cit.*) the mother may make the simple and dramatic statement that one or more of her infants has "turned blue, sighed and died".

'In the more usual type of case, the child is seized with screaming fits and attacks of colicky pain. During severe paroxysms the infant may straighten out its body and become rigid. Convulsions may occur. There is some vomiting and diarrhoea and the infant appears restless, pallid and ill. It may rapidly become worse—it is in fact in an acutely dangerous condition—but the disease may not prove immediately fatal and may follow a more chronic course. One very characteristic sign, usually encountered only in fairly severe cases, is partial or complete aphonia. The infant's cry may be thin and almost inaudible and in some instances it may go through the motions of crying, without any sound proceeding from its mouth. The aphonia, sometimes accompanied by signs of bronchitis, may suggest that respiratory disease is the primary cause of the infant's condition and confuse the diagnosis. Oedema is not a common feature. Textbook accounts of infantile beri-beri usually include a picture of a swollen cedematous infant and such pictures have, in my opinion, often hampered the recognition of the disease. According to some writers there may be localized cedema in certain cases, e.g. of the face, but this has not yet been observed in the series of cases treated in Cocanada. Enlargement of the right side of the heart and loss or diminution of the knee jerks are said to occur in some cases, but neither of these signs is easy to detect in a screaming and restless infant. Excoriation of the skin and mucous membrane at the angles of the mouth and in the region of the anus appears to be a fairly common sign. It has been observed in Cocanada but has not been recorded by other writers.

'In the more chronic form of infantile beri-beri, the clinical picture does not greatly differ from that of chronic malnutrition and marasmus of a less specific kind. There is pallor, vomiting, constipation, loss of

*The epidemiology of beri-beri in India has been fully considered in various papers from the Nutrition Research Laboratories. The prevalence of beri-beri in the Northern Circars is due to the fact that in this area machine-milled raw rice is consumed by all sections of the population.

weight and retarded growth. The nutritional disorders may be complicated by bronchitis or other infections. It is easy to understand how a condition originally caused by one particular dietary abnormality may become one of generalized malnutrition through failure to retain and assimilate milk in sufficient quantities.'

Since infantile beri-beri as described resembles other forms of disease and malnutrition among infants, the therapeutic test is of primary diagnostic importance. The injection of 2 milligrams or thereabouts of vitamin B₁ has a remarkable and dramatic effect on infants suffering from the disease. Within 24 hours the change for the better is unmistakable. The screaming fits and paroxysms cease, the infant appears placid, and its general appearance has visibly improved. A few more injections, given at intervals of one or two days, will complete the cure for the time being. Sometimes even infants who appear moribund can be saved by this treatment.

Work of the infant-welfare centre

Curative.—Up to the end of April 1945, 1,145 infants suspected of suffering from vitamin-B₁ deficiency have been treated by injections of vitamin B₁. The infants were breast fed and ranged in age from 1 to 12 months. The highest incidence was among infants aged 2 to 4 months, and most of the acute cases occurred in infants under 6 months. About 8 per cent were acute fulminating cases, and 7 per cent 'chronic'; the remainder may be described as sub-acute. The 'chronic' form was most commonly seen in infants over 6 months. The majority of mothers showed mild signs of peripheral neuritis, e.g. pain and tingling in the extremities and weakness of the extremities. Some were, however, free from such signs. A history of having lost previous infants from 'anasa' was common throughout the series. The majority of the mothers belonged to the poorer classes, and were living on a diet mainly composed of machine-milled raw rice.

Of the infants treated, 980 were discharged as cured. The condition recurred, however, in 68 of these, after intervals varying from 15 days to 3 months. Further similar treatment of recurrent cases was successful. It was noted that recurrence was uncommon among infants of mothers who were given tablets of vitamin B₁ as a daily dose.

At the date in question (31st March, 1945), 135 infants were under observation and treatment. Sixteen infants died in spite of treatment and 14 infants could not be traced after incomplete treatment. Those that died were mostly infants brought to the clinic in a very acute or even moribund condition.

Preventive.—An attempt was made to prevent the occurrence of vitamin-B₁ deficiency in infants by supplying vitamin B₁ tablets to mothers for 3 months before delivery and 6

months after it. The mothers were given a daily tablet containing one milligram of the vitamin during this period. Some mothers have received this prophylactic treatment, and its effects have been observed as far as possible. In one group of 54 mothers who gave a previous history of having lost babies from 'anasa' and showed evidence of peripheral neuritis, vitamin-B₁ deficiency occurred in 28 infants in spite of prophylactic treatment; this, however, readily responded to injection of the vitamin and no deaths occurred. A small group of 12 mothers with a similar history were given no prophylactic treatment and kept under observation; eight living children were delivered and all of these developed infantile beri-beri which was successfully treated. A high incidence of vitamin-B₁ deficiency was also observed in the infants of mothers showing no evidence of peripheral neuritis but giving the familiar history of previous deaths from 'anasa', whether vitamin B₁ tablets were given or not. A considerably larger group of mothers—some 500—who were free from signs of peripheral neuritis and gave no history of previous infant losses from 'anasa' were also observed. The incidence of vitamin-B₁ deficiency in the infants of these mothers was much smaller than in the groups mentioned above, and the administration of vitamin B₁ tablets to mothers appeared to have some preventive effect. Some mild cases did, however, occur in infants whose mothers received treatment. The general impression gained from these observations is that the regular administration of one milligram tablets of vitamin B₁ to expectant and nursing mothers is of some value in prophylaxis, and modifies the severity of symptoms in infants who develop this disease, but that such a dosage is too small for satisfactory prevention. The women given treatment were, in general, living on a diet grossly deficient in the vitamin and a supplement of one mg. daily fails to meet entirely the demands imposed by pregnancy and lactation, and to give infants complete protection from the danger of vitamin-B₁ deficiency.

A striking feature of the work of the centre has been its growing popularity. In the early stages attendances were relatively small, and many women in the town preferred to take infants suffering from the dreaded 'anasa' to quacks. But it was gradually learnt that an effective cure for 'anasa' was available at the centre, and attendances have gradually risen until at the present time 50 or more mothers, bringing their infants, attend daily. (Not all the infants, of course, are suffering from vitamin-B₁ deficiency.) The disease, as has been previously pointed out, is prevalent throughout the Northern Circars and women from towns as far distant as Vizagapatam have brought infants for treatment. The following table shows the numbers of infants from towns other than Cocanada treated for vitamin-B₁

deficiency, and the distance of these towns from Cocanada :

Name of place	Number of cases	Distance from Cocanada (miles)
Vizagapatam ..	27	103
Ellore ..	14	99
Pittapur ..	12	12
Rajahmundry ..	11	36
Ramachandrapur ..	8	20
Samalkota ..	7	8
Narasapatnam ..	6	80
Anakapalle ..	4	83
Razole ..	3	40
Bezwada ..	2	135
Yellamanchili ..	2	70

Public health policy

The work carried out to date has established the fact that infantile beri-beri is common in Cocanada and neighbouring areas. The proportion of all infants born that develop beri-beri, and the quantitative effect of the disease on the infantile mortality rate, have not yet been ascertained ; it is hoped to obtain data on these questions. The fact has, however, been clearly established that infantile beri-beri is an important public health problem which calls for suitable public health measures. There would be no obvious difficulty in establishing treatment centres for infantile beri-beri throughout the beri-beri area. Vitamin B₁ in tablet form is cheap and available in quantity. At the Cocanada centre infants have been treated by injection of the vitamin, which produces better and quicker results than administration by mouth. Ampoules purchased in the market are considerably dearer than tablets containing an equivalent amount of the vitamin, but a solution could be put up cheaply in bottles for subcutaneous administration.

Prevention by the use of the synthetic vitamin is a more difficult problem. The dosage required, and the necessary period of administration to mothers, have yet to be satisfactorily established. Its routine distribution to expectant and nursing mothers throughout a large area would require considerable organization, and the task of accustoming the people to this method of prevention would be a difficult one. The all-round improvement of the diet, so that it contains less rice and more pulses and other foods, would be the best method of eradicating the disease, but this can be achieved only by long-term measures to adjust and increase agricultural production and improve the economic condition of the people. The possibility of increasing the amount of vitamin B₁ supplied through the medium of the staple food, rice, must be carefully considered. The raw rice at present consumed is not highly milled, since the rice milling order of the Government of Madras prohibits the double polishing of rice. It is clear, however, that the rice at present con-

sumed does not supply enough vitamin B₁. In some families the rice purchased through the government ration shops is pounded in the home with the object of removing the pericarp that remains after milling and making it whiter. This may be one of the reasons why the milling order has not effectively prevented infantile beri-beri. Further, as Swaminathan (1942) has shown, the washing of raw rice removes as much as 60 per cent of the vitamin B₁ previously present. It is possible that the kind of raw rice at present in supply; while richer in vitamin B₁ than highly polished raw rice, is deprived of so large a proportion of its vitamin-B₁ content by washing and cooking that it falls below the danger-point when consumed as the principal article of diet. All these questions require investigation. No information is available as to whether the rice milling order has reduced the incidence and severity of infantile and adult beri-beri in the Northern Circars ; it has probably done so. The present investigation, however, shows that it has not effectively prevented infantile beri-beri.

Parboiled rice even after milling and washing, generally speaking, contains enough vitamin B₁ to prevent beri-beri, as is shown by the epidemiology of the disease in India. The popularization of parboiled rice in the beri-beri area has been advocated as a method of preventing beri-beri. 'Converted' rice, which is essentially similar to parboiled rice in its nutritive properties, would have the same effect. The people are, however, fully accustomed to raw rice and dislike parboiled rice, so that it would be difficult to bring about such a change of habit.

It has been clearly shown that infantile beri-beri is an important public health problem in the part of Madras in which adult beri-beri has long been prevalent. While the latter is unquestionably rare in areas in which parboiled rice is the staple food, it is not impossible that infantile beri-beri occurs in mild form in the infants of mothers consuming such rice. It is important that this question should be brought to the notice of those concerned with the care of infants in rice-eating areas outside the beri-beri area. The treatment of infants who are ailing from no obvious cause by injections of vitamin B₁ would throw light on this question.

Whatever the prospects of preventing infantile beri-beri by general improvement in the diet or by a change in the nature of the rice used as the staple cereal, efforts should be made in the meantime to make curative treatment by the pure vitamin more widely available. This offers a means of saving many infant lives, improving the health of infants, and preventing unnecessary suffering.

Summary

(1) A public health experiment which has as its objective the treatment and prevention of

infantile beri-beri is proceeding in Cocanada. The work has been carried out at an infant-welfare centre in that town.

(2) It has been found that infantile beri-beri is a common disease in breast-fed infants. It can be successfully treated by the injection of pure vitamin B₁.

(3) An attempt was made at prevention by the administration of the vitamin to expectant and nursing mothers, the prophylactic dose being 1 milligram of vitamin B₁ daily. While this treatment was not without effect, the dosage employed appeared to be too small for the fully effective prevention of vitamin-B₁ deficiency in infants.

(4) The public health aspects of the problem are discussed, and it is recommended that cura-

tive centres should be established elsewhere in the beri-beri area.

Acknowledgments

Thanks are due to Dr. Thompson Wells, Roche Products, Ltd., Bombay, for the liberal supply of Binerva ampoules and tablets. We must also thank Dr. W. R. Aykroyd, Director, Nutrition Research Laboratories, Coonoor, who initiated the inquiry and has been closely associated with it, for his help in drafting this paper.

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Current Topics

Inactivation of Malarial Parasites by X-Rays

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXVII, 21st April, 1945, p. 1058)

THE selective sensitivity of various diseased tissue to x-rays has important medical implications. Recently Bennison and Coatney tested the sensitivity of some species of malarial parasites to x-rays. *In vitro* both the sporozoite and the trophozoite forms of an avian malarial organism were found to be sensitive to x-rays. Of the two, the sporozoite form could be more easily inactivated. While doses of x-rays of less than 10,000 roentgens do not cause inactivation of the trophozoite form, there was a somewhat increased survival time of infected chicks. Also there was a noticeable increase in time after injection of infected blood before the birds showed positive blood smears. With this sensitivity in mind infected birds were irradiated, and under the conditions used there was no significant change in the survival time. *Plasmodium malariae* was irradiated *in vitro* and this treated blood then injected into a patient suffering from syphilis of the central nervous system. In the following thirty-two days no symptoms of malaria developed and no parasites were found in the blood smears. It appears that the organisms had been completely inactivated under the conditions of irradiation. The subject was later treated with the unirradiated blood and developed typical malaria. The prolonged prepatent period and also the increase in survival time of the chicks receiving the irradiated organism suggests that some of the parasites were totally inactivated, thus leaving only a small number to initiate the infection. It is believed that the cells most sensitive to x-rays are those in the process of division. It may be possible to inactivate selectively the malarial organism while it is in the process of reproduction. This would be difficult with the avian strain used, since all stages of the cycle are present in the blood stream at one time. However, in the highly synchronous infections with *Plasmodium malariae* of man practically all the parasites at a given time are at the same stage of development and one of these phases may well be sensitive to x-rays.

Methylene Blue Test for Urinary Bilirubin

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXVII, 21st April, 1945, p. 1058)

A SENSITIVE test that would reveal the prejaundice stage of liver damage would be useful. In 1933, Fellingner and Menkes described a method for the quantitative

determination of bilirubin in the urine with methylene blue. The qualitative test as described by Myers consists in adding two drops of Loeffler's methylene blue to 10 c.c. of urine. The solution remains dark blue if negative but turns a brilliant green if positive. The test is immediate and is not changed by temperature or the acidity or alkalinity of the urine. It can be read in natural or artificial light. In determining the quantitative value of the methylene blue test a method of simple dilution of the urine was done routinely. To keep the volume at 10 c.c., 1 c.c. of urine was replaced by 1 c.c. of water for the first dilution, 2 c.c. of urine by 2 c.c. of water for the second dilution, and so on until a negative test was obtained. In all cases in which positive methylene blue tests of the urine occurred, a serum bilirubin test was done immediately. Of the 59 cases of elevated serum bilirubin found among a group of employees exposed to tetrachlorethane, not one was found in which the methylene blue test of the urine was negative at the onset. The test was used on patients hospitalized for acute toxic hepatitis. Urine specimens were obtained each day on which a serum bilirubin test was done. The peak of the rise of bilirubin in the urine was present several days before the bilirubin in the serum reached its highest level. As improvement occurred, the urine became negative more promptly than the serum reached its normal level. More information is necessary to evaluate accurately the methylene blue test. Judging from the cases reported it is valuable in detecting early liver damage and thus avoiding further exposure to the toxic tetrachlorethane fumes.

The Indian Journal of Medical Research, Vol. XXXII, No. 2, October 1944

THE following is the list of contents:—

- (1) Kirwan, E. O'G., Sen, K., and Bose, N. Vitamin-B₁ deficiency as a cause of eye diseases in Bengal.
- (2) Sarma, P. S. The estimation of pyridoxine (vitamin B₆) in foods using rice-moth larvae (*Corcyra cephalonica* St.).
- (3) Kamala Bhagvat and Devi, P. Anti-thiamine factor in carp.
- (4) Kamala Bhagvat and Devi, P. Inactivation of thiamine by certain foodstuffs and oil seeds. Part I.
- (5) Kamala Bhagvat and Devi, P. Inactivation of thiamine by certain foodstuffs and oil seeds. Part II.



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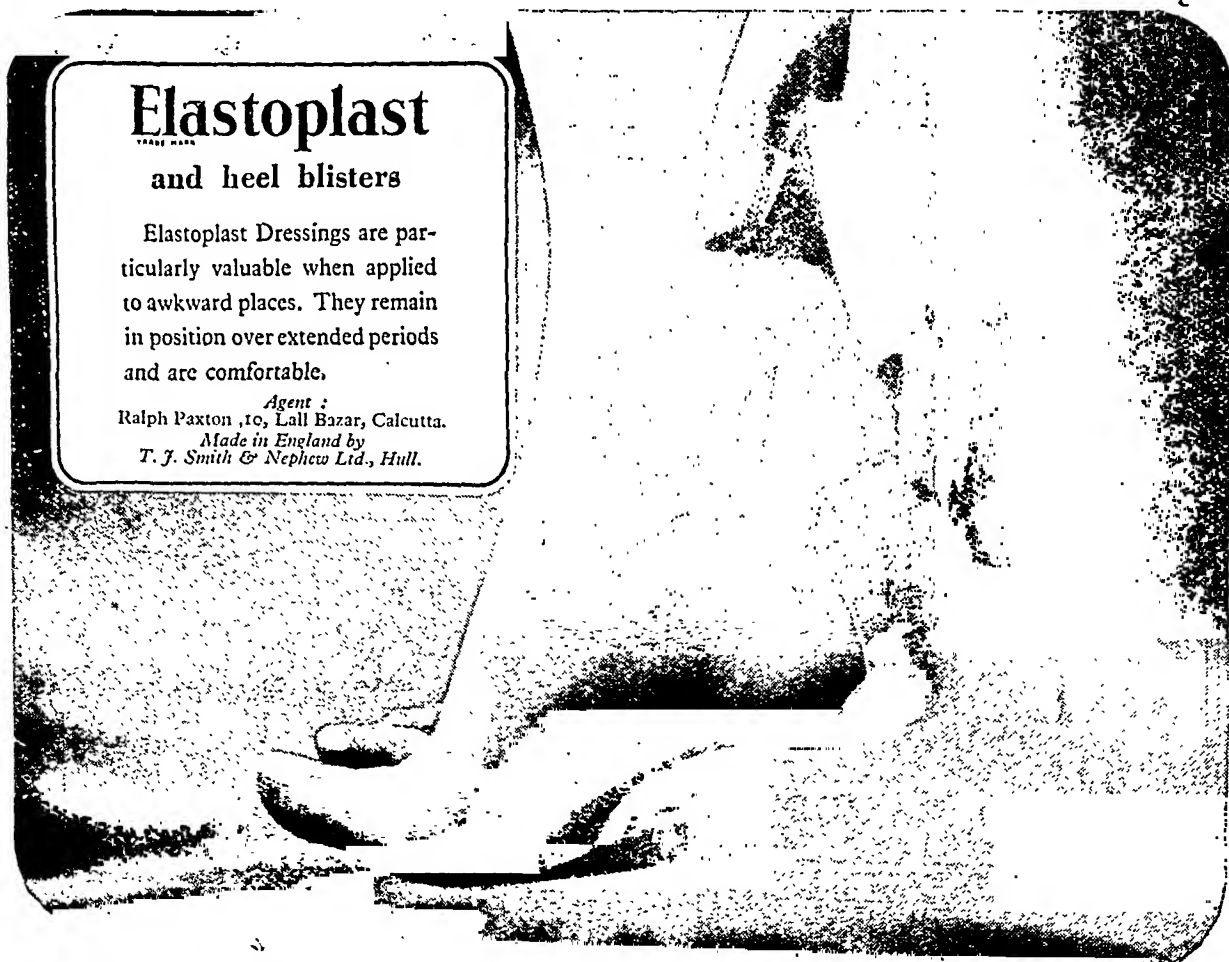
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- (6) Kamala Bhagvat and Sreeramamurthy, V. V. Liberation of tyrosine, tryptophane, cystine and arginine from proteins.
- (7) Sarma, P. S. Egg-white injury (induced biotin deficiency) in rice-moth larvæ (*Corcyra cephalonica* St.).
- (8) Rao, S. Dattatreya. Studies on the destruction of vitamin A in shark-liver oil. Part I. Destruction during normal storage: standardization of Pulfrich photometer for the estimation of vitamin A.
- (9) Rao, S. Dattatreya and Banerjee, B. N. Studies on the destruction of vitamin A in shark-liver oil. Part II. Development of acidity during storage of livers.
- (10) Ivengar, N. K., Bose, B. C., and Mukerji, B. Vitamin C in pine needles.
- (11) Setna, S. B., Sarangdhar, P. N., and Ganpule, N. V. Nutritive values of some marine fishes of Bombay.
- (12) Bhatia, B. B., and Kapur, R. D. Pharmacological action of alkaloids of *R. serpentina* Benth. Part I. Neo-aimaline and iso-aimaline.
- (13) Gupta, J. C., Kahali, B. S., and Dutt, A. The hypnotic effect of a resin fraction isolated from root of *Rauwolfia serpentina* Benth. obtained from Dehra Dun.
- (14) Kulkarni, R. N. Quantitative estimation of common trihalogen volatile anæsthetics in blood and tissues of animals.
- (15) Dharmendra and Mukherji, N. Attempts to transmit human leprosy to splenectomized monkeys.
- (16) Dharmendra and Mukherji, N. The effect of sulphapyridine on experimental rat leprosy.
- (17) McDonald, S. A method for the demonstration of Negri bodies.
- (18) Veeraraghavan, N. A protozoan parasite of the central nervous system.
- (19) Lucas, R. B. Isolation of a strain of *Rickettsia orientalis* from cases of XK tnhus in Ceylon.
- (20) Ahuja, M. J., and Brooks, A. G. *In vitro* test for assay of potency of cobra antivenene.
- (21) Ranganathan, S. Studies on experimental fluorine poisoning in rats.
- (22) Reddy, D. V. S., and Sastry, P. B. Studies in vital capacity.

The following are the authors' summaries and conclusions:—

(1) The incidence of riboflavin deficiency in Bengal is low.

The occurrence of ocular complications due to riboflavin deficiency is rare.

Among the small number of cases of vitamin deficiency with ocular complications observed, three responded to treatment with vitamin A.

It would seem that cases of angular stomatitis, with lesions of the tongue and scrotum, are due to deficiency of more than one vitamin.

(2) A larval method for the estimation of pyridoxine in foodstuffs and biological materials has been developed, based on the growth increase of pyridoxine-deficient rice-moth larvæ (*Corcyra cephalonica* St.).

The increase in growth of pyridoxine-deficient larvæ was proportional, with the range of 0.0 μ r. to 1.0 μ g. of pyridoxine per g. of diet, to the amount of vitamin present in the diet.

About thirty foodstuffs and biological materials have been analysed for their pyridoxine content by the larval method. The values are in good agreement with those obtained by Swaminathan's chemical method or by various animal assay methods.

Cereals and pulses, particularly the latter, are generally fairly rich in pyridoxine. Milk, meat, vegetables and fruits are poor sources of the vitamin.

Pseudo-pyridoxine, which is more active than pyridoxine in promoting the growth of lactic acid bacteria, has the same growth-promoting effect on rice-moth larvæ as pyridoxine itself.

(3) Carp muscle, viscera and blood were found to contain a factor which inactivated thiamine and which was extracted by chloroform-water mixture.

The factor has been found to behave like a typical enzyme in being thermolabile, its activity being dependent on the relative concentrations of the enzyme and the substrate thiamine.

Visceral extract and blood were found to be about 26 times richer in this enzyme than muscle extract.

The visceral and muscle extracts have lost their activity after dialysis for 48 to 72 hours. Activity could be restored by the addition of the boiled original extracts—suggesting the presence of two fractions, one heat-labile and non-dialysable and the other heat-stable and dialysable.

The enzyme was precipitated by full saturation of the muscle extract with ammonium sulphate. On dialysis, the precipitate was found to lose all its activity. The enzyme was also precipitated by 3 volumes of acetone, but this treatment was found to yield an unstable preparation of the enzyme.

The enzyme has been found to destroy thiamine present in dried yeast and animal tissues.

The carp enzyme is different from the anti-thiamine factor of ragi and mustard seed though certain similarities between them have been observed.

(4) Certain foodstuffs, viz. ragi, rice polishings, green gram, mustard seed, cotton seed and linseed were found to contain a factor which rapidly inactivated thiamine *in vitro*.

This factor (anti-thiamine) was shown to be soluble in water but insoluble in salt solutions and was extracted with chloroform-water mixture.

It was found to be non-enzymic in nature.

On dialysis, the factor was resolved into two components one heat-labile and non-dialysable and the other heat-stable and dialysable. Either component was active towards thiamine.

Destruction of thiamine in materials rich in thiamine, viz. brewer's yeast, was observed when the factor was mixed with them.

(5) The destruction of thiamine by ragi extract was confirmed by biological experiments with (a) larvæ of the mosquito, *Aedes albopictus*, (b) rats, and (c) pigeons.

Mosquito larvæ were found to utilize the breakdown products of thiamine produced by the action of ragi extract, though they were unable to utilize breakdown products of thiamine obtained by autoclaving, or by sulphite or NaOH treatment of the vitamin.

Rats and pigeons when fed with ragi extract to which thiamine was added in amounts adequate for their growth, developed signs characteristic of thiamine deficiency which were relieved by administration of thiamine.

(6) Seven proteins prepared from a variety of sources, after 18 to 20 hours hydrolysis (as recommended in the older methods), were analysed for 4 essential acids, viz. tyrosine, tryptophane, cystine and arginine.

Complete liberation of the above amino acids was achieved by hydrolysis of the proteins in the autoclave for 30 to 45 minutes at 15-lb. pressure and at 120°C.

The results given by the new procedure agreed well with those given by earlier methods.

Recovery of cystine and arginine added to protein solutions prior to autoclaving was good.

Tapioca protein was found to contain the essential amino acids in question in adequate amounts.

(7) Egg-white injury can be produced in rice-moth larvæ by feeding them on a diet containing raw egg-white. The larvæ fed on such a diet die off in about 4 weeks.

The toxic factor in raw egg-white is destroyed by mild acid hydrolysis, and by peptic digestion. The toxicity is not lost on denaturation with strong alcohol.

The toxic factor, which is present in the protein fraction, is present in an avidin concentrate prepared from raw egg-white.

The growth response of biotin-deficient larvae appears to be proportional to the amount of biotin present in the diet.

(8) The vitamin A in commercial samples of shark-liver oil is gradually destroyed on keeping. A systematic inquiry into the causes of the loss and the methods of preservation is necessary.

The Pulfrich photometer has been standardized for the estimation of vitamin A in shark-liver oil by the Carr-Price reaction. The factor for converting B into international units per gramme is 910 (average).

Provided the mean of a number of readings is taken, the Hilger vitamer A gives results as reliable as the spectrophotometer. In low potency oils there is considerable irrelevant absorption in the ultra-violet region.

(9) Though the vitamin-A potency remains practically unaffected during the preservation of livers with salt, the free fatty acid content, colour and odour of the resulting oil increase rapidly. Preliminary mincing of the livers appears to retard these undesirable changes considerably. To produce a high grade oil livers should be rendered within a very short time after landing the sharks.

* (10) This paper gives the results of analysis of 28 kinds of fish and crustacea of Bombay and points out the low cost of first-class protein obtainable from dog-fish and other despised varieties as compared with the cost of protein obtained from the more popular fishes as well as meat.

(11) The pharmacological action of two new alkaloids of *R. serpentina* (isolated from plants grown in the Dun valley) provisionally named as 'neo-ajmaline and iso-ajmaline' has been reported.

Both the alkaloids are found to have a slight stimulant action on the nervous system, followed by well-marked depression.

Both the alkaloids are found to have a depressant action on plain muscles of the heart, blood vessels and intestines.

Both of them lower the blood pressure in the intact, spinal and decerebrate animals in normal condition and also after experimental hypertension.

Neo-ajmaline has a powerful stimulant action and iso-ajmaline has a mild depressant effect on the uterus of rabbit and guinea-pig.

The average toxic dose of neo-ajmaline in frogs is 0.1 mg./g. body-weight, and for guinea-pigs is 0.065 mg./g. body-weight. Iso-ajmaline is slightly more toxic. In every case death was due to respiratory failure.

(12) From the crude 'resin' of *Rauwolfia serpentina* Benth. a fraction insoluble in petroleum ether but soluble in alcohol has been isolated. This is pharmacologically active.

In experimental animals (cats, rabbits, rats, frogs, guinea-pigs) it produces a sedative and hypnotic effect very similar to that produced by the standard extract of *Rauwolfia serpentina*.

The sedative action induced by the standard extract and also by the alcohol-soluble fraction described commences about 3 to 4 hours after administration and persists for more than 24 hours.

The 'resin' or alcohol-soluble fraction does not cause a fall of blood pressure but stimulates the simple muscle of the intestine and uterus. This action is produced immediately.

The petroleum-ether-soluble 'oil' obtained from the crude 'resin' prepared from *R. serpentina* has irritant properties.

(14) A sensitive method for the determination of small quantities of trihalogen anaesthetics in the blood by air distillation has been described. The anaesthetic and the lethal concentrations of trichlorethylene and chloroform were determined for various animals. The results obtained by this method were found to agree with those obtained by Buckmaster and Gardner for chloroform. The same method was also used to determine the anaesthetic concentrations in various organs, e.g. liver and brain. The rate of disappearance

of the two anaesthetics after cessation of anaesthesia was also determined.

(15) It has not been possible to transmit human leprosy to splenectomized monkeys. Thus we have not been able to confirm the report of Cochrane *et al.* regarding the possibility of infecting splenectomized monkeys with human leprosy. However, our method of inoculation differed from that of Cochrane *et al.*: they introduced a piece of leprosy nodule and fixed it to the splenic stump, while we injected leprosy material intraperitoneally some days after splenectomy.

In none of our monkeys were acid-fast bacilli found at the post mortem. It is a well-recognized fact that the lepra bacilli, even the dead bacilli, have remarkable powers of persistence in tissues of living animals. The failure to find some of the injected bacilli in our monkeys is believed to be due to the long interval that elapsed between the inoculation and the post mortem. It appears that the injected bacilli do not persist for periods as long as three years or more.

The results of the lepromin test, performed with the nucleoprotein of the Hansen's bacillus, show that none of our monkeys had been sensitized to the products of this bacillus, even after being inoculated twice. It appears that the number of bacilli contained in the amount of suspension injected (10 c.c. in two injections) was not sufficient to sensitize the animals; other workers have reported the development of an allergic state after repeated inoculations.

(16) It appears that rats with an average weight of 80 gm. cannot tolerate orally an initial daily dose of 40 mg. to 50 mg. of sulphapyridine. However, after preliminary treatment with small repeated doses the animals can tolerate this dose quite well.

Under the conditions of the experiment described herein, sulphapyridine has failed to modify the course of experimental rat leprosy in white rats. The drug does not appear to have an inhibitory effect *in vivo* on *Myc. lepræ muris*, although *in vitro* it has been shown to have a bactericidal effect in a 1 in 1,000 dilution.

We have thus failed to confirm the work of Krakower *et al.* (*loc. cit.*), who reported that the feeding of sulphanilamide modified the course of the disease to a great extent, only small leprosy lesions appearing in the treated rats, whereas large leprosy lesions and extensive metastasis developed in the untreated control rats. Our findings are in keeping with the findings of Cowdry and Ruangsiri (*loc. cit.*), who found that repeated subcutaneous injections of promin did not modify the course of the disease in any way.

* (17) A technically simple and satisfactory method for the demonstration of Negri bodies is described.

(18) A parasite, apparently protozoal in character, originally found in the mid-brains of guinea-pigs experimentally infected with rabies 'street' virus has been studied and a full description of its morphology has been given.

An account has been given of the occurrence and behaviour of this protozoal parasite in other animals.

Appearances, similar to the various stages in the life-cycle of the parasite described, have been observed in the mid-brain of dogs and jackals suffering from natural rabies infections and in the brains of experimental animals infected from them.

Certain stages in the life-cycle of the protozoal parasite described appear to be 'filtrable'; it has been possible to produce evidence of infection in experimental animals by the inoculation of brain suspensions passed through Berkefeld V and N candles.

The protozoal parasite described appears to be a specific infection of the central nervous system, and, in spite of exhaustive searches, it has never been observed in other organs and tissues.

This parasite has never been observed except in association with natural or experimental rabies infection.

The possibility of the protozoal parasite described being connected with the aetiology of rabies has been discussed.

The possible relationship of this parasite to Negri bodies has also been discussed and the suggestion has been put forward that Negri bodies may represent a stage in the life-cycle of the parasite.

(19) The isolation of a strain of *R. orientalis* is described.

The white mouse is considered to be the experimental animal of choice for this type of work.

Guinea-pigs, in the majority of cases, contract an inapparent infection when inoculated with *R. orientalis*. This state of inapparent infection has been transmitted through four generations of the animals.

Attempts to infect the yolk sac of the developing chick embryo failed.

(20) An *in vitro* test is described for the estimation of the anti-haemolytic titre of cobra antivenene. The anti-haemolytic potency of the immune serum corresponds closely with its anti-neurotoxic titre as determined by the *in vivo* test on pigeons.

(21) Further experiments were carried out on the effect of calcium salts on fluorine poisoning.

The different salts of calcium have roughly the same potency in mitigating the toxic effects of fluorine. Magnesium salts too confer a similar protection, though to a somewhat smaller degree.

The toxicity of fluorine compounds cannot be accounted for by their solubility in water; magnesium fluoride was found to be the most toxic, followed in descending order by sodium fluoride and calcium fluoride.

Vitamin C did not lessen the severity of fluorine poisoning rats.

Vitamin D had no beneficial effect on rachitic conditions superimposed on fluorosis.

(22) Vital capacity was measured in 310 male subjects of different sects, classes and ages. The average capacity was 2.985 c.c.

Various anatomical measurements such as height, weight, etc., have been correlated with vital capacity. The highest correlation was obtained between sitting height and vital capacity. Chest expansion gave the next best relation. No correlation was found between age and vital capacity.

A table showing the results recorded by different Indian workers and English, American, Chinese and Japanese averages has been given.

Penicillin by Mouth

(Abstracted from the *Medical Press and Circular*, Vol. CCXIII, 25th April, 1945, p. 258)

GIVEN by mouth in the ordinary way, penicillin is inactivated by the gastric juice. Lederle Laboratories Inc. have now produced 'penicillin pills'. The penicillin is suspended in oil and encased in a gelatine capsule. The gelatine is dissolved in the stomach and the penicillin in oil, little affected by the gastric juice, passes on into the duodenum to be absorbed. These capsules are reported to have been tried on both men and animals in a New York hospital with equally good results. They are said to remain stable at room temperature for months without detectable loss of potency. If this report (as we believe it to be) is well founded, it should mean that patients in future will be able to receive penicillin in their own homes in the same way as the sulphonamides, or any other drug, without having to go into hospital. They will also avoid a considerable amount of pain, and the third result we foresee will be an enormous extension of the use of penicillin by the profession generally.

Penicillin Therapy in Skin Infections

By N. M. WRONG

MAJOR, R.C.A.M.C.

(Abstracted from the *Canadian Medical Association Journal*, Vol. LII, April 1945, p. 341)

PENICILLIN was used with the following base: lanette wax SX, 25 per cent; paraffin oil, 10 per cent; water,

q.s. ad 100 per cent. Strength 250 units per gramme of base.

Quite arbitrarily, it was decided to apply the penicillin emulsion every four hours, six times in 24 hours (q. 4h. \times 6) for three or four days or until definite clinical improvement was noted, and then reduce the frequency to q. 8h. \times 3 for the remainder of the treatment. After a short time on this regimen the frequency was reduced to q. 6h. \times 4 for the first three or four days and then q. 8h. \times 3 for the balance of the treatment.

The organisms were identified—streptococcus, staphylococcus, etc.—and if staphylococci were found the coagulase test was performed to evaluate pathogenicity. Then all organisms present were tested for penicillin sensitivity by the ditch-plate method described by Fleming. It is a waste of a valuable agent to use penicillin to treat infections caused by a penicillin-resistant organism, therefore, this preliminary investigation must be done in every case. Nothing will discredit penicillin more than its indiscriminate use.

The routine adopted was to use saline compresses only while the bacteriological studies were being completed. Then, if the case was suitable, the crusts were bathed of, the pustules opened aseptically and penicillin emulsion was applied thinly with a sterile wooden tongue depressor. The emulsion must be kept at ice box temperature at all times when not in use and care must be taken to avoid metal containers and contamination, hence the sterile wooden tongue depressor. Face, neck and ears were left uncovered but arms and legs were usually lightly covered with clean gauze after the emulsion was applied.

DURATION OF TREATMENT AND RESULTS

1. *Impetigo of face, ears and scalp*.—(a) Uncomplicated: average duration of treatment 9½ days.

The results were extremely good. Within 24 or at most 48 hours all weeping and crusting had ceased and the patient was comfortable. Underlying inflammation of the skin took several days to clear but, apart from redness, the patient's skin appeared normal by the third or fourth day. If treatment was then discontinued relapse occurred. To prevent this, treatment was continued for an average of 9½ days.

(b) Complicated by seborrhœic dermatitis, otitis externa, eczema or sulfonamide dermatitis, average duration of treatment 12 days.

The results were not nearly as striking as in the uncomplicated series. The infection was quickly controlled but the underlying dermatitis persisted so that recurrence was common. Frequently the co-existing dermatitis had to be treated by x-ray before the skin returned to normal.

2. *Folliculitis of beard (sycosis barbæ)*.—Average duration of treatment 12 days.

The immediate response to treatment in this disease was very dramatic. Some patients who had suffered from papules and pustules in their beard for months or years, notwithstanding numberless treatments, were completely clear in four or five days and remained so as long as treatment was continued. However, in this series relapses were very common.

3. *Ulcerative impetigo of upper and lower extremities (ecthymatous ulcers, 'desert sores')*.—Average duration of treatment 10 days; (a) uncomplicated. The results of treatment were most successful of all. Within 72 hours the patient was free of discomfort and the ulcers were clean, dry and filling in. By the end of a week, most of them were healed but treatment was continued for three more days to prevent relapse.

(b) Complicated by varicose dermatitis, eczema, impetiginous dermatitis and sulfonamide dermatitis, average duration of treatment 14 days.

In these the results of therapy were much less striking than in the uncomplicated ones and the tendency to relapse was greater. In several, injection or ligation of varicose veins was performed after clearing the infection with penicillin and the patient was then returned to duty. In others, x-ray therapy was used

to clear the residual eczema, impetiginous dermatitis or sulfonamide dermatitis.

Penicillin Failures

(From the *United States Naval Medical Bulletin*, Vol. XLIV, May 1945, p. 1083)

THAT penicillin is not a panacea is well established. Until the exact chemistry of the agent is known, what the drug will or will not do is dependent upon bio-assay measures which are as empiric as the original chance discovery of the substance. That it is not a single pure chemical is apparent from recent extraction and fractionation methods employed in its production.

The partitioning into several components was brought about by crystallization of each product of the various methods of culturing penicillium notatum: that grown in flasks and spoken of as super facial culture produces an active substance designated as penicillin F and identified by British workers as penicillin I, that grown in tanks, the submerged culture, is penicillin G (penicillin II), and that which is grown superficially but extracted by chloroform is penicillin X (penicillin III or allopenicillin). Two other fractions have been identified, penicillin IV and penicillin V. The possibility of others in the remaining fluid is not excluded. Furthermore, there is evidence which suggests that each fraction has therapeutic specificity. It is certain that as far as activity against the gonococcus is concerned, the G fraction is less active than crude penicillin, whereas penicillin X is more active than either.

How much any one factor is present in the marketed ampoule is not indicated on the label nor is the method of production stated. Fractional assaying, moreover, has not been considered practical up to the present date.

From the method of production the tank-submerged culture gives the most abundant yield and as a consequence is the substance commonly employed therapeutically. Inasmuch as this penicillin is composed almost exclusively of factor G it is obvious that the therapeutic properties of the ordinary commercial penicillin are mostly commensurate with those of factor G, and the term 'penicillin' practically connotes penicillin G.

However, the proportion of the individual constituent factors is not consistent and one lot of commercial penicillin may have more penicillin G in it than another, notwithstanding the fact that the two were grown simultaneously from the same parent mold in different tanks or successively in the same tank. Similarly, proportions of penicillin F, X, IV, V and others vary in each batch. Obviously penicillin produced by different manufacturers will show further variables.

Implications of these findings are apparent and may explain the success or failure of penicillin in comparable pathologic conditions. For the same reason it is impossible to state that the effectiveness or ineffectiveness of any lot of penicillin now on the market is attributable to the presence or absence of any particular penicillin constituent.

These facts may also explain the therapeutic variations observed in the British and American products and moreover may account for the apparent contradiction regarding the efficacy of single-dose medication. Successful results in eradicating gonorrhoea with a single intramuscular injection of penicillin X have been demonstrated. On the other hand, the single-dose failures recorded in the literature may be because of insufficient quantities of allopenicillin in the product administered.

The import of these findings cannot be over-emphasized and indicate the need of a rechecking of all therapeutic records before any final appraisal of penicillin can be made. The uncertainty of the proportional composition of the various factors in the penicillin employed makes this task impossible but

points to the course required of all evaluation studies of penicillin failure.

Purification and fractionation by crystallization is going on to a limited extent at the present time and permits accumulation of experimental data regarding the activity of the penicillin factors on different strains of micro-organisms. Until each fraction, however, can be produced in commercial quantities, the crystalline crude penicillin now employed must satisfy all therapeutic demands, its complexity making its limitations intelligible.

Clinical Thermometry

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXIV, 8th April, 1944, p. 1061. As abstracted in *Medical Bulletin*, Vol. XIII, 2nd June, 1945, p. 93)

How long does it take a clinical thermometer to record body temperature accurately? This question is discussed in the editorial of J. A. M. A. of the 8th April, 1944. In order to learn what schools of nursing are teaching with respect to asking temperatures, a questionnaire was sent to one hundred outstanding schools. According to the replies, twenty-seven schools taught their students that the time required for accurate registration was less than three minutes, thirty-seven stated three minutes and only five recommended an interval longer than three minutes. Many clinical thermometers on the market bear such designation as '½ minute', '1 minute' or '60 seconds', which obviously suggests to the user that the time required to register body temperature is that inscribed on the instrument.

On basis of a series of observations, the authors concluded that an insertion time of 3 minutes should be the minimum interval for oral clinical thermometers under ordinary conditions of use. Variations in the configuration of the bulb made no appreciable difference in time required to reach the final reading. The thermometer manufacturers should eliminate the time-designation on their instrument, because it is misleading. It is essential that sufficient time should be given to the thermometer to record accurate temperature.

Transmission of Infection During Withdrawal of Blood

By K. MENDELSSOHN

and

L. J. WITTS

(Abstracted from the *British Medical Journal*, i, 5th May, 1945, p. 625)

WHEN blood is taken from a vein with a syringe by the orthodox technique some of the blood is sucked back into the vein when the tourniquet is released. If, therefore, the syringe is not sterile the patient is exposed to infection.

Treatment of Severe Starvation

(From the *British Medical Journal*, i, 5th May, 1945, p. 634)

IN 1939 Elman and Weiner reported the use of an acid hydrolysate of casein fortified by the addition of tryptophan and by supplementation with cystine or methionine for intravenous alimentation of human subjects; evidence was obtained of satisfactory utilization of the amino-acids, and favourable therapeutic effects were observed. The work of Elman and Weiner constituted a practical application of the observation of Henriques and Andersen in 1913 that nitrogen equilibrium could be maintained in the goat when the sole source of nitrogen was provided by the intravenous administration of amino-acids. During the last few

years numerous papers have appeared dealing with the clinical use of hydrolysates of protein for alimentation either by the intravenous or oral routes; most of these referred to the use of the American product 'amigen', a pancreatic hydrolysate of casein, and it has been stated by Allbright that complete maintenance can be effected with 'amigen' and glucose alone for as long as forty days. Some attention has also been paid to acid hydrolysates and to digests of meat prepared with papain. The ideal preparation is yet to be found; pancreatic digests are highly susceptible to bacterial contamination during their production and are therefore liable to be pyrogenic; papain digests, while relatively free from this disadvantage, may contain partial breakdown products of protein which are harmful, and the acid hydrolysates require fortification with tryptophan, which is not a very easily accessible substance. The only report so far published on the use of protein hydrolysates in the treatment of starvation has come from India; a considerable measure of success was claimed as the result of intravenous administration of papain digests of meat together with glucose to patients who were so far weakened by starvation that they were unable to take anything by mouth. The Indian work was undertaken in conditions of such difficulty that a carefully controlled investigation was not possible, and the evidence for the favourable effect of intravenous alimentation rests on clinical observation only.

The food situation in the Netherlands is exceedingly grave. This applies particularly to the large towns of North-West Holland, where there is good reason to believe that few people have been getting more than 800 calories and where they may now be getting only about 400 calories daily. After considering the data available the Netherlands authorities and the military authorities concerned agreed that the food situation in N.-W. Holland was so serious that special measures would be required if a large proportion of the population were to be resuscitated; being impressed by the evidence in favour of the use of protein hydrolysates, they invited the Medical Research Council to advise on the provision of suitable preparations in adequate quantity. At the same time a scheme for the application of the emergency treatment was agreed upon with the Netherlands authorities; this scheme included not only the formation of relief teams but also full provision for clinical and laboratory study of the cases of extreme starvation, so that the best method of treatment might be determined without delay. As the result of work carried out during the last eighteen months the Medical Research Council was in a position to give the necessary technical advice, and in view of the urgency of the need the Ministry of Food and the Ministry of Supply took immediate steps to increase production; with the whole-hearted co-operation of the firms concerned the amount of material which was asked for was produced in less than the specified time. Since it also seemed desirable to test the efficacy of plasma and serum in the treatment of extreme starvation, large supplies of these materials were requested and were furnished by the Lister Institute. The work in Holland is now in progress. Representatives of the Medical Research Council and of the Ministry of Food, together with American experts, are acting, at the invitation of the Netherlands Government, as scientific advisers.

It is now depressingly apparent that the problem of treatment for extreme starvation is of wide extent; it concerns a proportion of British prisoners of war and large numbers of occupants of enemy concentration and labour camps. Quite recently the Medical Research Council, at the request of the military authorities, has nominated a further team of three experts to proceed to the Continent to study the value of protein hydrolysates in treatment of starvation; this team is already at work with full equipment for the investigation required. Provision has also been made, at the request of the Ministry of Health, for material to be available for repatriated prisoners of war who

may reach E.M.S. hospitals in urgent need of treatment. All these demands have increased the need for medical personnel, and use has been made of Belgian and English medical students who were enrolled, trained, and organized in anticipation of such a need. Two methods of treatment were considered. In the first a solution of protein hydrolysate, which may be prepared by complete enzymic digestion ('amigen') or by acid hydrolysis and subsequent fortification with tryptophan, is given by intravenous infusion. The second method consists in administration of the hydrolysate by slow intragastric drip, and in this case the material is an enzymic digest of casein or meat in which the digestion has not been carried so far. In both cases glucose is given in large amount to provide energy and thus to spare the amino-acids for purposes of repair. Vitamins are also given to enable the glucose to be utilized and to prevent the development of acute deficiency states. It is anticipated that successful treatment should lead within three days to resuscitation to the point at which ordinary food may be taken.

It is impossible at the present stage to predict the ultimate value of the protein hydrolysate treatment in extreme starvation, although there is already evidence that the intractable diarrhoea which is a prominent feature of the condition responds well to the intravenous method. It is much to be hoped that the intragastric drip will prove to be a satisfactory alternative form of administration; if so it will become the method of choice, not only because suitable material is so much more easily accessible but also because its use will be free from the risks which, at present at least, seem inseparable from the intravenous administration of hydrolysed proteins. Apart altogether from the prospect that the availability of protein hydrolysates may provide a valuable therapeutic measure in the present medical emergency, the studies which will be carried out offer the promise of useful information for the future; the observations which are made may be expected to have a bearing not only on the immediate problem but also on the treatment of all conditions of malnutrition associated with impaired absorption from the alimentary tract.

The High Nutritive Value of Skim Milk

By R. C. HUTCHINSON

(Abstracted from the *Medical Journal of Australia*, Vol. I, 5th May, 1945, p. 457)

SKIM MILK IN HUMAN NUTRITION

In a report from the League of Nations it is stated that 'the special nutritive value of milk lies in its mineral and protein content and this is in no way reduced through the removal of the butter fat'. Actually, skim milk contains more mineral matter and protein than whole milk, and the removal of the fat is frequently advantageous. Because of its low fat content, skim milk leaves the stomach more rapidly than whole milk, and, consequently, much larger quantities of skim milk can be consumed before an uncomfortable feeling of fullness is experienced.

During the past decade a number of experiments have been conducted, in which skim milk has supplemented the diets of children with favourable results.

Skim milk containing 1 per cent of fat and added lactic acid has been found of value in the following conditions, principally the first: (i) in diarrhoeal diseases in artificially fed infants; (ii) for premature and debilitated infants for whom breast milk is unobtainable; (iii) to supplement breast milk when this is insufficient; (iv) for infants who do not tolerate whole milk; (v) in the treatment of habitual vomiting.

THE COMPOSITION OF SKIM MILK

The average composition of skim milk is given in table I. Fresh skim milk is comparatively low in total solids, but its high nutritive value does not depend upon a high concentration of solid matter so much as

on the unusual properties of its individual constituents. In addition to being a carbohydrate with a high nutritive value, lactose possesses the unique property of transforming the intestinal flora from one in which Gram-negative putrefactive organisms predominate to one consisting almost exclusively of Gram-positive acidophylic types. Milk protein, consisting of casein, lactalbumin and lactoglobulin, contains every amino-acid discovered to date. All the essential mineral elements are to be found in skim milk, which is man's best source of calcium.

TABLE I
Major constituents of skim milk

Constituent	Fresh, per cent	Concentrated, per cent	Powdered, per cent
Lactose ..	4.9	14.7	50.9
Milk protein ..	3.5	10.5	36.4
Mineral matter ..	0.8	2.4	8.3
Milk fat ..	0.1	0.3	1.0
Vitamins ..	+	+	+

Fresh, concentrated and powdered skim milk contain approximately 36, 107 and 372 calories per 100 grammes, respectively.

CONCLUSION

Every available wholesome food should have a permanent place in the national dietary, and the place occupied by skim milk should be very prominent—not as a substitute for whole milk, but as a valuable supplement when adequate supplies of whole milk are too expensive or not available.

Agranulocytic Angina Effectively Treated With Intravenous Pyridoxine (Vitamin B₆)

By M. M. CANTOR

and

J. W. SCOTT

(Abstracted from the *Canadian Medical Association Journal*, Vol. LII, April 1945, p. 368)

BLOOD transfusions, so commonly used in this disorder, are described by Piney as useless and even dangerous. Pentose nucleotide has many advocates, but the dosage required, the long latent period before any improvement is noted, and its frequent ineffectiveness suggest that it is not a specific and that a remission might have occurred without its used.

Liver extract by the intravenous route is a more recent development. The clinical response to liver is difficult to assess because so often it has been combined with other measures. Experimentally, the reports are more promising.

It is thus clear that granulocytopenia in rats, which develops as a result of the administration of sulfonamides or thiourea, responds to liver or some liver extracts. Waisman and Elvehjem suggest that 'folic acid' is the active agent in this liver fraction. Daft and Sebrell provide experimental evidence for this view. In a critical review of this development, it is pointed out that the effect of folic acid may be indirect, in that folic acid is required by the coliform bacteria in the intestine for the production of some accessory substance which in turn produces the granulocytopenic response.

Since pyridoxine is a constituent of liver and yeast, Vilter, Schiro and Spies administered pyridoxine intravenously to three pellagrins and two patients with pernicious anaemia in relapse. Improvement was noted within 48 hours, and although there was only a 5 per cent reticulocyte response, there was a striking increase in the leucocyte count, especially in the granulocytic

series. Goldman and Malvados report somewhat similar observations in bone marrow studies on three cases of Cooley's anaemia. These findings led us to attempt the treatment of agranulocytic angina with intravenously administered pyridoxine.

The rapid and uniform response noted in our patients treated with pyridoxine hydrochloride intravenously (200 mg. daily) leads us to propose that:—

1. Pyridoxine is the factor in liver and liver extracts responsible for the granulocytopenic effect noted when liver is administered in agranulocytic angina.

2. Pyridoxine produces granulocytopenia by an effect on the myelocytic elements of the bone marrow. It seems probable that pyridoxine is the factor involved in the maturation and emigration of the polymorphonuclear leucocyte.

Clinical Malaria in Wartime

By F. R. DIEUAIDE

LIEUTENANT-COLONEL

(Abstracted from the *War Medicine*, Vol. VII, January 1945, p. 7)

1. No known drug prevents infection with malaria.

2. Both quinacrine hydrochloride and quinine rapidly suppress all clinical symptoms and trophozoite parasitaemia, no matter how many previous treatments. Small doses of quinacrine hydrochloride with suitable initial loading reliably prevent the appearance of symptoms.

3. No known drug by any method of use cures *P. vivax* malaria, i.e. prevents relapses. On the other hand, quinacrine hydrochloride does cure *P. falciparum* malaria.

4. The incidence of relapses in persons with *P. vivax* malaria cannot be shown to be influenced significantly by any known drug. After standard treatment with quinacrine hydrochloride, however, the average remission is much longer than after treatment with quinine.

5. The toxic effects of quinacrine hydrochloride when properly administered are neither serious nor troublesome. Those of quinine, though usually not serious, are somewhat more troublesome.

6. Quinine possesses no advantage over quinacrine hydrochloride except possibly more easily obtained rapidity of action in critical emergencies. It possesses certain disadvantages already indicated.

A highly qualified officer stationed in a malarious theatre recently wrote that he believed the Army to be better off for not having an unlimited supply of quinine.

Of pamaquine naphthoate it may be said that:—

1. It is useless in clinical attacks.

2. Its toxic effects are serious and frequent.

3. Army experience has given no evidence that it significantly affects the incidence of relapses in *P. vivax* malaria.

4. In highly endemic areas where natives are not extensively treated, the destruction of gametocytes of *P. falciparum* (the outstanding action of pamaquine naphthoate) is futile. The short duration of *P. falciparum* infections after treatment with quinacrine hydrochloride makes the use of pamaquine naphthoate in the United States rarely necessary.

Synthesis and Destruction of Nicotinic Acid by the Mixed Cæcal Flora of Man

By R. BENESCH

(Abstracted from the *Lancet*, i, 9th June, 1945, p. 718)

HUMAN faeces obtained from a caecostomy was cultivated aerobically and anaerobically, the nicotinic-acid content of medium flux culture being estimated at intervals for nine days.

Under aerobic conditions a considerable synthesis of nicotinic acid took place, mainly after the third day of cultivation.

Under anaerobic conditions the caecal organisms destroyed two-thirds of the nicotinic acid present in the original medium.

It is suggested that in the normal caecum an equilibrium is struck between organisms which produce and those which destroy nicotinic acid. An upset in this equilibrium may play a part in the causation of deficiency diseases.

Reviews

A POCKET SURGERY.—By Philip H. Mitchlner, C.B.E., T.D., M.D., M.S. (Lond.), F.R.C.S. (Eng.), D.Ch., Hon. (Durham), D.L., and A. H. Whyte, D.S.O., M.B., M.S. (Durham), F.R.C.S. (Eng. and Edin.). 1943. J. and A. Churchill Limited, London. Pp. vii plus 272

THIS small volume embodying the essentials of various surgical injuries and diseases along with the outstanding points of diagnosis and treatment of these conditions, was meant to supply the medical officers in the services with a concise *vade mecum* of the subject. The scheme adopted in Romanis and Mitchiner's Science and Practice of Surgery was followed. The book was undoubtedly of help to those for whom it was intended. In the period that has elapsed since the publication of this book there have been advances of outstanding importance particularly in the treatment of infections by penicillin and newer sulphonamides. Inclusion of these and a revision of the sections dealing with the infections and surgical conditions peculiar to the tropics will greatly enhance the value of this Pocket Surgery to general practitioners and the medical students.

P. C. S. G.

THE VASCULAR ABNORMALITIES AND TUMOURS OF THE SPINAL CORD AND ITS MEMBRANES.—By Roger Wyburn-Mason, M.A., M.D., B.Chir. (Cantab.), M.R.C.P. (Lond.), M.R.C.S. (Eng.). 1943. Henry Kimpton, London. Pp. vii plus 196, with 42 illustrations. Price, 18s.

THE subject of vascular anomalies and tumours of the spinal cord had attracted little attention in the past. This was because of the difficulty in the clinical diagnosis of these conditions, and the failure to recognize the various types of vascular anomalies and tumours that occur in the spinal cord. This monograph, embodying the result of Dr. Wyburn-Mason's painstaking researches on this interesting subject, is an important contribution to neurology. It will draw the attention to the frequency and the importance of these anomalies and provide a basis for the accurate diagnosis of these conditions. Dr. Wyburn-Mason's use of kymography with the use of lipiodol intrathecally is a very interesting and valuable contribution to the methods of investigation of neurological diseases.

The printing, get-up and the illustrations are excellent. The appendix containing the full clinical notes of 67 illustrative cases will greatly facilitate the understanding of the clinical features of these pathological conditions.

The book will be read with great interest and profit by all neurologists.

P. C. S. G.

DISEASES OF THE NERVOUS SYSTEM. DESCRIBED FOR PRACTITIONERS AND STUDENTS.—By F. M. R. Walshe, O.B.E., M.D., D.Sc., F.R.C.P. (Lond.), Hon. D.Sc. (Nat. Univ., Ireland). Fourth Edition. 1945. E. and S. Livingston Limited, Edinburgh. Pp. xvi plus 360. Illustrated. Price, 15s.; postage, 7d. (Home)

The fourth edition of Dr. Walshe's excellent handbook on neurology has been thoroughly revised in the

light of the recent progress in knowledge of the subject. The chapters on peripheral nerve lesions, herpes zoster, cervical rib, sciatica and protrusion of the intervertebral disc have been recast and new matter on the nature of aetiology and the concept of psychosomatic illness have been included. Of the new therapeutic methods and remedies and diagnostic methods, only those of proved value to the clinicians have been included.

P. C. S. G.

THE RHEUMATIC DISEASES.—By G. D. Kersley, M.A., M.D. (Cantab.), F.R.C.P. (Lond.). Second Edition. 1945. William Heinemann (Medical Books), Limited, London. Pp. xii plus 120. Illustrated. Price, 15s.

THE second edition of Dr. Kersley's book has been thoroughly revised and largely rewritten in the light of the advances in knowledge and technique. The preventive and industrial aspects of the rheumatic diseases have been discussed. A new chapter on the inter-relationship and aetiology of the rheumatic diseases has been added, as also chapters giving brief descriptions of types of specific infective arthritis and of conditions simulating arthritis. The experiences of the war, which have brought newer methods of treatment into use, particularly those that have proved of value in the treatment of diseases such as sciatica and fibrositis, have been adequately described.

This concise and informative volume will prove of value to the senior medical student and the general practitioner.

P. C. S. G.

THE DIABETIC LIFE: ITS CONTROL BY DIET AND INSULIN: A CONCISE PRACTICAL MANUAL FOR PRACTITIONERS AND PATIENTS.—By R. D. Lawrence, M.A., M.D., F.R.C.P. (Lond.). Thirteenth Edition. 1944. J. and A. Churchill Limited, London. Pp. xxiii plus 228, with 18 illustrations. Price, 10s. 6d.

DR. LAWRENCE'S book 'The diabetic life' is one of the best on the subject. In this edition the writer has rewritten the whole book in the light of recent advances on the subject. Problems of diabetics arising out of food rationing and war conditions have been adequately dealt with.

This edition will undoubtedly continue to be as popular and valuable to the physician and the intelligent diabetic patient as the previous editions.

P. C. S. G.

THE REHABILITATION OF THE INJURED: OCCUPATIONAL THERAPY.—By J. H. C. Colson. 1944. Cassell and Company, Limited, London. Pp. xvi plus 226, with 196 figures in the text. Price, 15s.

THE book is devoted entirely to the use of physical therapy in the after-treatment of various injuries, fractures, dislocations, etc. Various measures of specific or remedial occupational therapy, diversional occupational therapy are described in full detail with excellent illustrations. The rationale of the various movements involved in the different specific remedial occupational therapeutic measures are explained; this is of importance for, unless the surgeon or the physiotherapist can explain the rationale of the exercises to the patient, there is, as the author states, a risk of truculent remark from the patient, e.g. 'And how much do we get paid an hour for this, Gov'nor? I thought this was a treatment centre—not a bloomin' concentration camp'.

The book contains nine parts arranged in 25 chapters; the different parts and chapters dealing with aims, general principles and applications, with resettlement in employment, with certain handicrafts such as knotting, netting, tablet weaving, seating, basketry, weaving and fretwork, with woodwork, with gardening, with domestic work, and with timber work. The book will be of great interest to surgeons and physiotherapists, and to those engaged in the practice of

diversional and occupational therapy of the countless injured victims of the World War II.

P. C. S. G.

ANNUAL REVIEW OF BIOCHEMICAL AND ALLIED RESEARCH IN INDIA. Volume XIII for 1942. Published by the Society of Biological Chemists, India, Malleswaram P. O., Bangalore. Pp. 101. Price, Rs. 3 or 6s.

This small volume contains a review of the scientific researches on biochemical and allied subjects in India in 1941-42. The individual chapters have been devoted to enzymes; vitamins; general nutrition; human physiology; animal nutrition; protein, fat carbohydrate and mineral metabolism; pharmacology; human pathology; plant physiology; chemistry of plant products, soils and fertilisers.

The chapters present well-balanced reviews of the contributions on the subjects. The book will be read with considerable interest by the workers on the subject in India and abroad.

P. C. S. G.

THE PROBLEM OF SICKNESS AMONG WOMEN IN INDUSTRY. 'PAMPHLET NO. 3.'—Issued by the Industrial Health Research Board of the Medical Research Council. Published by His Majesty's Stationery Office, London. Pp. 22. Price, 4d.

This pamphlet is divided into two parts. The first part analyses the results obtained from the records of cases contained in Report 86 under the following points: How much loss of time does illness cause; the main types of illness; number of cases of each type of illness; length of absence in each type of illness; effect on output of each illness; sickness absence any (i) age among married and single women, (ii) length of service, (iii) working conditions, and (iv) shift systems. The summary of this analysis is as follows:—

The records covered a period of six months, in five factories, and are not a suitable basis for wide generalizations. There is an urgent need for industry to keep records of sickness absence on a wider and more uniform scale. This necessarily limited inquiry showed that:

1. 7.8 per cent of the total working time was lost through sickness absence, and sickness absence accounted for at least half of the total time lost.

2. Two-thirds of the sickness absence was caused by only 16 per cent of the workers.

3. The illnesses which caused most lost time were the respiratory, 'nervous' and 'fatigue' and digestive diseases.

4. Young married women had a particularly high rate of sickness absence, especially for 'nervous' and digestive illnesses.

5. Women who had been working since the beginning of the war lost more time and had longer absences through sickness than women who had had shorter service.

6. There is some evidence that workers on production, and also shift workers, were particularly liable to sickness absence.

The second part of this pamphlet analyses the interviews with workers on the following points: shift work, and sickness absence and life outside the factory. The summary of this analysis is given below:

1. Most shift workers disliked the idea of changing from the arrangement of shifts to which they were accustomed.

2. The lack of a proper week-end break in shift work made the workers tired, bored and discontented.

3. Night work was definitely liked by one-third of the women, and also definitely disliked by one-third.

4. The main reasons for dislike of the night shift were the inability to sleep well, alleged poor ventilation in the factory at night, digestive troubles, longer hours, and the disturbance of family life.

5. Weekly hours of work were not overlong, except for a minority of workers, and it was the arrangement rather than the number of hours which caused most dissatisfaction.

6. Transport and domestic duties presented fewer problems than in the earlier days of the war, but women with full domestic responsibilities had more than the average amount of sickness absence.

7. About half the women had personal worries, and worry was associated with a high rate of sickness absence.

MEDICAL RESEARCH COUNCIL WAR MEMORANDUM NO. 10. Second Edition. 'The medical use of sulphonamides.' By various authors. London: His Majesty's Stationery Office. 1945. Price, 1s. 3d. net.

The sulphonamides have occupied an important place in medicine for several years. Various attempts have been made in the past to prepare comprehensive accounts of the uses of these drugs. With the rapid developments that have been taking place previous accounts have been out of date a few months after they had been written. Now, however, sufficient time has elapsed to make it possible to prepare a report on the uses of the sulphonamides which have now been fairly thoroughly worked out and on which there is now general agreement. It is therefore gratifying to receive from His Majesty's Stationery Office a copy of the Medical Research Council's War Memorandum No. 10 on the medical use of sulphonamides. This report with appendices and index runs to 71 pages. The memorandum was originally issued in 1943 on behalf of the committee of the Medical Research Council whose chairman was Professor L. J. Witts. The memorandum was drafted by a body of six well-known medical men and with the advice of numerous others. In the second edition many of these authors and advisers have taken a hand and new material has been contributed by a number of workers. This edition, as was the previous edition, has been edited by F. Hawking and F. H. K. Green. It contains sections on chemistry, pharmacology, general considerations and the relationship of penicillin therapy; on dosage and its regulation and toxic and other harmful effects. There are 14 sections on the treatment of specific infections and there are brief notes on the uses of sulphonamides in other conditions. There is also a note on the prophylactic use of sulphonamides, and appendices covering the estimation of sulphonamides in body fluids, bacteriological studies and sterilization of sulphonamide powders. There is also a useful index.

MEDICAL RESEARCH COUNCIL. SPECIAL REPORT SERIES NO. 250. CHRONIC PULMONARY DISEASE IN SOUTH WALES COAL MINERS. III. Experimental Studies. 1945. Published by His Majesty's Stationery Office, London. Pp. 84. Illustrated. Price, 5s.

The Medical Research Council undertook an investigation of chronic pulmonary disease in South Wales coal miners in 1936. Two reports, one on the medical survey and related pathological studies and the other on environmental studies, have already been published [vide reviews in *I.M.G.* (1) LXXVII (1942), p. 699 and (2) LXXIX (1944), p. 141]. It was suggested that difference in the dust might have something to do with variations in the incidence of pneumokoniosis, and this led to further research.

The present report includes accounts of the analysis of the mineral deposits found in the lungs of workers in South Wales coal field, of an experimental study of the tissue reactions produced in the lungs by selected dusts and of a study of the solubility of such dusts.

From post-mortem investigation of lungs of 54 workers it was found that the composition of the lung residue varied for different occupational groups, but significantly more quartz was found in the 'silicotic nodulation' category than in the less severe fibrosis groups. There are reasons for dismissing mica or kaolin and accepting quartz as the major aetiological agent in the production of pneumokoniosis. From the experimental study of the effects on the lungs of rats of different specimens of dust, it appears that pure

coal dust causes little fibrosis but the pathogenicity becomes greater as its silica content increases. When quartz dust is mixed with coal, the resultant confluent fibrosis is more like that seen in pneumokoniosis in coal workers than that characteristic of the effect of pure quartz dust.

The data presented in these reports suggest that difference between the pneumokoniosis of local workers and the classical silicosis (as seen, for example, in sandstone workers) is due to small amounts of quartz being mixed, in the former case with large amounts of coal and other minerals. But still there are some points which are not quite clear, e.g. the pathogenicity of some siliceous dusts and the relative harmlessness of others, the relation of their solubility to toxicity, etc. The Council propose to put in hand further investigation as soon as possible.

R. N. C.

MEDICAL RESEARCH COUNCIL. INDUSTRIAL HEALTH RESEARCH BOARD REPORT NO. 88. 'A STUDY OF WOMEN ON WAR WORK IN FOUR FACTORIES.'—By S. Wyatt. Assisted by R. Marriott, W. M. Dawson, N. M. Davis, D. E. R. Hughes and F. G. L. Stock. 1945. Published by His Majesty's Stationery Office, London. Pp. 44. Price, 9d.

THE Industrial Health Research Board of the Medical Research Council have been carrying out a series of investigations on the problem of sickness absence in women working in the factories and the results of these investigations have been reported from time to time, e.g. Report 4 'A study of absenteeism among women', Report 69 'Incentives in repetitive work', Report 77 'Fatigue and boredom in repetitive work', Report 86 'A study of certified sickness absence among women in industry'. In Report 86, the sickness records of 1,000 women selected at random in each of five factories were analysed from the standpoint of the type, frequency and amount of absence, and their relation to such factors as age, length of service, civil state, and type of work. The present report (no. 88) is an extension of this investigation and gives the results of interviews with 100 women from four of the random samples previously chosen; in one factory a second group of 100 women were interviewed at a later date. Each group of 100 women consisted of the 50 who had had the most frequent and lengthy periods of sickness absence during the last six months and the 50 who had had the least sickness absence in this period. Each interview lasted from 30 to 60 minutes and was conducted in a special room. The general aims of the interview were first explained to each worker and emphasis was placed on the confidential nature of the procedure. The report contains factual evidence and opinions expressed by the workers, analysed under the following heads: A. Inside the factory—environmental factors, personal relations, payment, pace of work, shift systems and hours of work, night work, and attitude to job. B. Outside the factory—transport, recreation, home life, and health. There is also a section on general considerations.

The summary of conclusions is as follows:—
The women now employed in industry vary considerably as regards home background, social status and previous experience, yet, judging from the sample included in this inquiry, they seem to have settled down to factory life remarkably well. On the whole, they were fairly satisfied with their jobs and with working conditions, and there were few general complaints. Worries and difficulties were usually local or individual and connected with specific factory conditions, and were less numerous and disturbing than those associated with home life. The attitude of the women to specific factors may be summarized as follows:—

Inside of factory

(a) Unsuitable atmospheric conditions, especially on the night shift, were a frequent cause of discomfort, and probably of reduced efficiency.

(b) Relations with other workers were very satisfactory, but contacts with supervisors, and still more with shop managers, were often remote or non-existent, and were unlikely to promote complete unity of aim and effort.

(c) A large majority (77.6 per cent) of the women were satisfied with the amount of payment, and a somewhat smaller proportions (62.1 per cent) with piece-work prices.

(d) The attitude to the pace of work was highly satisfactory, since only 8.8 per cent of the women were dissatisfied and most of these were employed in two factories.

(e) Approximately 50 per cent of the women were employed on the three-shift system with a weekly change of shifts, and a large majority appeared to be content with this arrangement. Of the three shifts, the morning shift was by far the most popular, and the night shift the least. As a rule, the women preferred to begin the day in the factory, and to have the later part of the day free.

(f) About one-third of the women rather liked night work, mainly because of the comparative absence of distracting and disturbing influences, and the chance to do things in daylight.

About 40 per cent of the women on night work had not more than six hours in bed, and some not more than four hours. Married women, on the average, had a shorter rest than single women. A large majority of the women on night work usually had a snack rather than a full canteen meal. There was some evidence that night work was associated with loss of appetite and digestive trouble.

(g) Satisfaction with work was more widespread among women who were formerly employed in the factory or in the home, and among volunteers rather than conscripts. Older women tended to be more satisfied than younger women, and married women more so than single. Some women found the work monotonous and meaningless, and about two out of every five felt they were contributing little or nothing to the war effort.

Outside the factory

(h) The average time for the single journey between home and factory varied from 27 to 41 minutes in the different factory groups. A majority (60.8 per cent) of the women were able to complete the journey in 30 minutes or less, and only 6.8 per cent took more than one hour. On the whole, the transport services were well organized, and there were few complaints.

(i) Only a moderate proportion (52.6 per cent) of the women were satisfied with the time available for recreation, and the proportion was less for married than for single women. Some women had enough time, but not enough energy or inclination, to enjoy their leisure. The main preventive factors were long or unsuitable hours of work, and household duties.

(j) Only two-thirds of the married women lived in their own homes; most of the remainder, and approximately two-thirds of the single women, lived with parents. Less than half the married women had children living at home, and very few had children under five years old.

Although only a minority of the women seemed to be overburdened with the practical domestic problems of house-work, shopping and the care of children, a larger number complained of home difficulties and appeared to be worried and unhappy in their home life.

(k) About 59 per cent of the women claimed to have had good health before entering the factory, and a somewhat smaller proportion (46 per cent) alleged that health had been impaired by factory work. Younger married women and older single women had the poorest health histories.

Approximately 50 per cent of the women had worries and anxieties, mainly connected with men folk overseas, health matters and home affairs.

(1) Sickness absence was more prevalent among married women (especially those under 35) than among single women. It was also associated with home duties and difficulties, lack of daytime sleep when on the night shift, and personal worries. Those with most sickness absence also felt more fatigued, both during and after work, and were more inclined to blame factory conditions for their ill health.

In general, the women in these factory groups seemed to be content if the wages and comfort reached reason-

able standards, if hours of work were not too long, and if they were not moved from their usual jobs. Not more than 2 per cent were seriously dissatisfied with their jobs and with everything connected with them, from 10 to 15 per cent were moderately dissatisfied, and most of the remainder were content. Most women seldom complained unless they were jolted by some unwonted circumstance from their accustomed grooves or were overwhelmed by home duties and worries.

Abstracts from Reports

REPORT OF THE SCIENTIFIC ADVISORY BOARD, INDIAN RESEARCH FUND ASSOCIATION, FOR THE YEAR, 1944

This report as usual gives details of the composition of its board and advisory committees during the year, the reports of the meetings held, and an authoritative account of the medical research carried out during the year. It also contains information on the *Indian Journal of Medical Research* and the *Indian Medical Research Memoirs*, a list of papers published under the auspices of the Indian Research Fund Association and the programme of work recommended for 1945-46. Some of the important points in connection with the major researches carried out during the year are indicated under the following main heads: cholera, malaria, nutrition, leprosy, plague, pharmacology, and other researches. For detailed and technical information the original report should be consulted.

Cholera.—Two enquiries were conducted under this head during the year:

(1) At the Calcutta School of Tropical Medicine on the treatment of cholera with sulpha drugs.—In a series of cholera cases treated with sulphaguanidine the evidence was in favour of sulphaguanidine. As these trials were not extensive, no definite conclusion could be arrived at. A small series of cholera patients under field conditions were treated with this drug with encouraging results. A number of laboratory tests were performed which showed that sulphaguanidine has a destructive action on the causative organism of cholera.

(2) Evaluation of anti-cholera inoculations in Madras.—The following is a summary of some of the data obtained and the conclusions drawn:

(i) In a population of about 3 millions exposed to the risk of contracting cholera there were 708,977 inoculated or protected persons, amongst these 1,128 cases of cholera occurred. In 2,119,568 uninoculated persons there were 34,336 cases of cholera. The incidence of cholera in these two groups was 1.57 and 16.20 per 1,000 respectively, *viz.* the incidence in the uninoculated was 10.3 times more than in the protected group.

Out of 2,350 villages under survey 627 villages had a second outbreak of cholera a month or more after the last case in the first outbreak. In these villages there were 541,808 uninoculated persons while the inoculated or protected persons numbered 281,484, the greater proportion of whom had been inoculated in the first outbreak. In the second outbreak 6,580 cases of cholera occurred in the uninoculated group and 241 in the inoculated group; the case incidence rates per 1,000 in the two groups being 12.14 and 0.86 respectively. The incidence in the uninoculated was 14.2 times more than in the inoculated or protected group. The uninoculated persons run 10 to 14 times greater risk of contracting cholera than the inoculated persons in a community.

(ii) In the whole survey, there were 1,118 cases of cholera with 474 deaths in the inoculated group, and 50,053 cases with 27,576 deaths in the uninoculated group, the case fatality rates in the two groups being

42.4 per cent and 55.1 per cent respectively. The advantage derived from anti-cholera inoculation is not so much in recovery from the disease, if one is unfortunate to develop it, as in not getting it.

(iii) The data obtained during the present investigation show that immunity is established as early as the third day after inoculation.

(iv) Among the villages which experienced a second outbreak of cholera, the intervals between the first and second outbreaks varied from 1 to 12 months. By classifying these villages according to the interval between the two outbreaks and comparing the cholera incidence during the second outbreak in the uninoculated group with that amongst persons inoculated in the first outbreak, the duration of immunity was determined. It was concluded that the immunity conferred by anti-cholera inoculation lasts for a minimum period of five months and that there is strong evidence to suggest that immunity lasts for 10 to 12 months.

(v) The data relating to the villages which experienced more than one outbreak of cholera showed that the greater the proportion of inoculations done in the first outbreak, the less the chances of cholera during the second epidemic wave. Thus mass immunity plays an important part in preventing the development of cholera epidemics.

MALARIA

The research activities of the Malaria Institute of India, Coonoor and Delhi, have been curtailed owing to the abnormal conditions brought about by the war. Laboratory research has been restricted mainly to the preparation of antisera for determining the source of mosquito blood meals. Two thousand one hundred and sixty-nine tests have been carried out by this method. The technique of the preparation of JSB water soluble strain has been modified to attain greater simplicity. A number of indigenous drugs were tested on monkey malaria, but none of these was found to have any parasitocidal value. A new ICI synthetic drug, M 3349, was also subjected to test in monkey malaria. While the parasites disappear from the peripheral blood after the 3rd dose of this drug, it in many cases did not prevent relapses of malaria in monkeys. The study of mosquito bionomics has been continued and the routine identification of mosquitoes and other insects of medical importance have been carried out as in former years. At the Southern India branch an extensive series of studies on the bionomics of certain anopheles was carried out. Laboratory colonies of certain important species of anopheles were maintained. A special strain of bird malaria parasite was also kept in the laboratory.

An extensive series of experiments, both in the laboratory and in the field, have been carried out in insecticides, such as Indian and foreign emulsions, activators of pyrethrins, individual sparklet sprayers, freon bombs, etc., repellents, such as pyrethrum cream, DMP cream and DMP liquid repellent have been tested. Experiments have also been conducted on DDT with various diluents both as larvicide and insecticide. A number of samples of cloth, camouflage netting, etc., have been investigated to ascertain their protective value against mosquito bites either when

sprayed with repellents or left unsprayed. The standard type of hand sprayer (MISH) has been modified in certain respects.

The inquiry into the methods of forecasting epidemic malaria at the Public Health Department, Punjab, Lahore, studied the basic data from which forecasts of malaria epidemics in the Punjab have been prepared during the past years. These data have been compiled on a monthly basis for the province as a whole and separately for 15 individual districts. During the process of compilation and charting it became evident that the annual epidemic figures of the province exhibited a periodicity of 8 or 9 years' duration. The main conclusions are that, in the Punjab, a significant decrease has occurred over the period of 77 years (1867-1943) in the annual epidemic figures, thus demonstrating that, with the passage of time, an increasing degree of control has been exercised on epidemics breaking out in the province. These methods strongly suggest the existence of an eight-year's cycle of malaria in the Punjab; but in view of the period studied being not of a sufficiently long duration, and in view of the rigidity of the technique employed in testing it, the existence of the periodicity has not been conclusively established. For purposes of forecasting, however, it seems necessary that due notice should be taken in future of the possibility of the occurrence of a malaria epidemic after a period of 8 years. In some cases this period might fall short by one year and in others the appearance of the epidemic might be delayed by one year. Some work has also been done on the assessment of the degree of relationship between the epidemic figure and rainfall in the case of Sialkot district. Whilst rainfall in August is highly correlated with the annual epidemic figure, the association is not satisfactorily significant with the rainfall in July.

Nutrition.—This important section of the report is the largest and covers 37 pages; the reports of the 11th and 12th meetings of the Nutrition Advisory Committee and of the sub-committees comprise another 39 pages.

Work done at the Nutrition Research Laboratories included: (i) the analysis of many different food-stuffs, yeasts and yeast extracts for vitamin B₁ and nicotinic acid content; a special method worked out in these laboratories was used. The effect of washing and cooking on the vitamin content of rice was studied. (ii) The use of certain oils and cereals reduced the vitamin content in the foods, particularly of B₁. This factor which destroys B₁ was studied. It consists of two components: one destroyed by heat and the other not destroyed by heat. Work is in progress to isolate these factors and to study the destruction of vitamins by certain chemical agents.

The amount of vitamin B₁ in a number of foods was determined by special methods. Cereals and pulses are good sources of this vitamin, while the foods usually designated 'protective' are often poor sources. Dried yeast is rich in this vitamin.

The nutritional requirements of three strains of lactic acid bacteria have been studied and it was found that vitamin-B complex is essential for primary growth. A number of samples of shark-liver oil were tested for vitamin A content. Studies have been made of the lasting properties of carotene in the various forms in which it is marketed. Opening of the container was followed by gradual destruction of carotene.

The use of tapioca is rapidly spreading in South-west India. The nutritive value of this root is therefore a question of practical importance. A diet largely composed of tapioca, unless supplemented by some source of additional protein, fails to support the growth of rats. Analysis has shown that tapioca protein is not deficient in essential amino acids; quantitative and not qualitative deficiency is the important factor. The proportion of rice in a diet based on tapioca which is needed to produce nitrogenous equilibrium in rats was determined.

Animal experiments: (i) Experiments with guinea-pigs have shown that vitamin P accelerates growth. A factor isolated from Bengal gram has a similar effect.

(ii) Work on experimental fluorosis was continued. Of the 3 fluorides it was found that calcium fluoride was the least toxic, next came sodium fluoride and the most toxic being magnesium fluoride. Experimental work in rats failed to support the previous conclusions that vitamin-C deficiency contributed to the causation of fluorosis in man. (iii) Studies of vitamin C production in rats have shown that the production is perhaps not affected by bacterial action in the gut. (iv) Attempts to make rats immune to rat leprosy by giving a highly nutritious diet failed. (v) Studies of the production of fatty liver in rats by giving low protein, high fat diet were carried out. No marked difference was found between the different fats and oils used. (vi) The development of rice moth larvae on different diets has been used as a method of studying the action of vitamins and amino acids and the relation between them.

Field investigations included studies of a form of nutritional diarrhoea seen in Madras which responded dramatically to injections of nicotinic acid, statistical analysis of the data obtained from the investigation of the relationship between dental caries and the fluorosis, and investigation of infantile beri-beri in Coochabed.

The ascorbic acid inquiry at the University College of Science and Technology, Calcutta, carried out a number of laboratory experiments on the biological synthesis of ascorbic acid under influence of narcotics using rats as experimental animals, with a view to elucidating the mechanism of this synthesis. A great amount of work of a highly technical nature and of basic importance was carried out.

The inquiry on plasma proteins in health and disease at the Grant Medical College, Bombay, studied 25 cases of nutritional oedema with the constant finding of a low albumin content of the blood. Some of the patients responded well to high protein diet. Numerous such cases were seen in Bombay and further careful studies of this condition are planned. Fifty cases of hyperproteinæmia were studied; the increase in the concentration of total protein being due to an increase in globulin. This is seen mostly in chronic disease such as kala-azar, tuberculosis, syphilis and liver disease.

The inquiry on the rôle of manganese in the biological synthesis of ascorbic acid at the Prince of Wales Medical College, Patna, report that manganese was found necessary for the synthesis of ascorbic acid from an investigation on guinea-pigs.

The inquiry into factors affecting normal calcium metabolism in certain areas in the Punjab at the Punjab University Institute of Chemistry, Lahore, investigated the composition of diets in certain parts of the Punjab, and the calcium, phosphorus and phosphatase contents of the blood serum in relation to diets. The studies indicated gross deficiency of calcium and a relatively high proportion of phosphorus in the diet. In Kangra much calcium deficiency was found, in Kulu little or none.

The inquiry on protein metabolism by human feeding experiments at the Public Health Laboratories, Bankipore, Patna, undertook the study of the protein content of different foods and its biological value, particularly to find out whether a mixture of rice proteins and pulse proteins increases their biological value. The mixture of rice protein and pulse protein was not found as effective as rice and milk protein. Feeding experiments have been started on two human subjects in order to find out the nitrogen balance of a mixture of cereals in a poor man's diet. The pulse and vegetable quota has been kept constant, but a mixture of rice and wheat, rice, wheat and maize, rice, wheat and barley, rice, wheat and milk has been given and the daily intake and excretion of nitrogen is being determined.

The inquiry on the deterioration of vitamin A in liver oils, concentrates and other preparations at the Indian Institute of Science, Bangalore, studied the deterioration of vitamin A in liver oils, concentrates and other preparations under different conditions of manufacture. The effect of storage, mincing, mixing

with salts, humidity, moisture, admixture of liver debris, mixture of other oils, were studied. Acidity particularly produces deterioration in vitamin-A content of shark-liver oil.

The inquiry into the relationship between vitamin-B complex and tumour growth at the Tata Memorial Hospital, Bombay, a study of the vitamin content of liver of different strains of mice susceptible and not susceptible to mammary cancer gave high values for insusceptible mice. The influence of butter-yellow, a tumour-producing agent on the vitamin content of the internal organs and on the development was also studied. The incidence of tumour in the experimental animal was much lower than that reported by previous workers in other countries. Metabolism studies were also carried out in 24 patients with oral cancer.

The inquiry into test of the biological value of soya bean protein, growth tests with soya bean, and human experiments with soya bean, at the Punjab University Institute of Chemistry, Lahore, showed that a definite improvement of the biological value of the proteins of soya bean and pulses on drying and heating and on improvement in the nutrient and growth-promoting value of the poor rice diet when soya bean or Bengal gram is added.

The Nutrition Research Unit at the Dacca University, Dacca, studied the rate of absorption in rats of various fats and oils, the inter-relationship between fat and calcium metabolism, the growth of young rats on different fats and oils, the stability of vitamin A in different oils, and the effect of a low fat diet in human subjects. The availability of iron in different food-stuffs was studied, and also the biological value of soya bean protein in different samples. Feeding experiments in rats showed improved growth with soya bean or pulses added to the diet. Some of the interesting findings are: (i) coconut oil possesses a decalcifying effect in man, (ii) among the common vegetable oils studied, groundnut oil produces the greatest increase in weight per gramme of the oil fed, buffalo butter fat is better than groundnut oil.

The Nutrition Research Unit at the Seth G. S. Medical College, Bombay, studied the effect of different levels of fat intake on the growth of rats, metabolism experiments of the different levels of fat intake, the effect of fat intake on reproduction, the absorption of fats from the intestine, the value of different varieties of soya bean, the analysis of certain foodstuffs not commonly used outside Bombay.

The inquiry into methods of treating sick starving destitutes in Calcutta based on the All-India Institute of Hygiene. Studies showed a high incidence of malaria (35 per cent), of bowel diseases (36 per cent), and various degrees of anæmia in sick destitutes (severe in 20 per cent, moderate in 61 per cent, and slight in 19 per cent). Biochemical investigations of the blood, and a careful investigation of the physical condition of the patients were carried out with a view to improving methods of treatment. Post-mortem material was also studied and the findings reported in detail.

Inquiry into the estimation of vitamin-A activity of plant foods at the Punjab University Institute of Chemistry, Lahore, studied 15 samples of maize of different varieties in the Punjab. The different active carotinoid pigments in plant foods were isolated and individually estimated. Similar studies in other plant foods have been undertaken.

The inquiry on the rôle of nutritional factors in hepatic cirrhosis at the Haffkine Institute, Bombay. Preliminary investigations carried out during 1931-1935 showed that 'alcohol appears to have a very insignificant rôle' and that 'dietetic deficiencies appear to be important factors in the causation of cirrhosis of the liver in the cirrars'. The diets of patients suffering from the disease were grossly deficient in protein, fat and vitamins especially vitamins A, B complex and C. During recent years, experimental evidence has accumulated to suggest that cirrhosis of the liver may be a deficiency disease. It has been shown in animals

that deficiency of protein and vitamins of the B₂ group occurs in liver damage.

Animals were fed on diets deficient in vitamin-B₂ complex to study the incidence of liver cirrhosis or damage and degeneration. As there is evidence to suggest that an amino acid, methionine, plays an important rôle in the prevention of liver damage, attempts are being made to isolate this substance.

The inquiry on the chemical nature and nutritional availability of food iron at the University College of Science and Technology, Calcutta, carried out a comparative study of egg-yolk iron and tissue iron and found some striking differences in their chemical behaviour. The blood-forming effect of nucleic acid on rats kept on milk diet was also studied. It was found that the supplementing of a basal milk diet with iron and nucleic acid enhanced the blood-forming power in the rat but does not promote growth.

The inquiry on poor rice diets and food preparations in common use in South India at the Women's Christian College, Madras. Rats were given as much as they could eat of the basal 'poor rice diet' consisting of parboiled milled rice (cooked) 89.7 per cent, Bengal gram (cooked) 3.0 per cent, brinjal 4.3 per cent, mutton 0.26 per cent, coconut oil 0.21 per cent, green plantain 2.1 per cent, gingelly oil 0.43 per cent. On this diet the growth was poor and the general condition as indicated by malformation of the hind legs, loose rough hair with extensive bald patches, and a marked susceptibility to lung disease, was also poor. The following were found to be valuable supplements: calcium and natural foods rich in calcium—milk, ragi, amaranth and other leafy vegetables. Curds, also a source of calcium, show less supplementary effect than unsoured milk, but this was partially explained by the appetite factor. 'Rasam' (pepper water) made from tamarind, onion and minute quantities of chillies, garlic, mustard, pepper, cumin and gingelly oil, one of the most common accompaniments of rice diets in South India, had no real supplementary value. The addition of fat to the 90 per cent rice diet, in the form of butter, ghee, shark-liver oil or vegetable oil, not only induced no supplementary effect on growth but worsened the general condition of the animals. Cholan and cambu substituted for part or all of the rice had insignificant supplementary effects, and little, if any, superiority over rice as the basic cereal. When ragi was used alone, the growth and condition of the animals were better than with any of the other cereals, but not so good as when used in combination with rice or with cholan.

Improved cheap modification of rice diet containing parboiled milled rice (cooked) 50 per cent, ragi (cooked) 20 per cent, Bengal gram (cooked) 10 per cent, amaranth 10 per cent, sprouted green gram 5 per cent, brinjal 5 per cent, and costing no more than the poor rice diet, gave strikingly better growth and improved general condition in animals, thus indicating that marked improvements can be made in poor institutional diets without increase in cost. Analysis of common food preparations in use in South India were also carried out.

LEPROSY

(1) The Leprosy Inquiry at the School of Tropical Medicine, Calcutta, has continued work on the several different lines. Cases of leprosy are divided into two groups, neural and lepromatous, and the clinical features, prognosis, etc., in these two groups are now well known and clearly defined. The neural cases show good prognosis and the lepromatous cases a relatively poor one. The clinical studies were mainly concerned with details of the relatively small number of cases which cannot be classified as either neural or lepromatous, and in which accurate prognosis is difficult. The value of the improved form of the lepromin test in classification and prognosis is stressed. Attempts to prepare from the leprosy bacilli, a substance which will give specific leprosy tests have not been successful, the test at present being of value in prognosis and not in diagnosis. Also attempts to prepare a reacting

substance of similar properties from acid-fast bacilli other than the leprosy bacillus have been unsuccessful. The specific nature of the substance isolated by other workers from the urine of bacteriologically positive cases has been investigated; the work completely failed to confirm the presence of any specific reacting substance.

Therapeutic studies have included a study of the use of iodized hydnocarpus oil instead of the creosoted hydnocarpus oil which is generally used, the creosote being no longer available.

Sulphapyridine which has shown an inhibitory effect on rat leprosy bacillus in the test tube was tested in rats with rat leprosy and was found to have no influence on the disease.

Epidemiological studies included a thorough leprosy re-survey of the area under the Leprosy Investigation Centre, Bankura. The re-survey showed little difference from the findings of the survey in 1937. There is no rapid increase in this area, one of the most highly endemic areas of India. Several thorough surveys of small selected areas in different parts of India have been carried out under the British Empire Leprosy Relief Association.

(2) The Leprosy Inquiry at the Lady Willingdon Leprosy Sanatorium, Chingleput, Madras, carried out epidemiological studies of leprosy in certain selected villages in North Arcot and elsewhere in the Madras Presidency with a view to preventive work. The factors influencing the spread of leprosy were: (i) close marriage relationship between a heavily infected village and one in which the incidence is low or non-existent. (ii) The mere proximity of a village to one in which there is a heavy incidence has no influence on the spread of leprosy in the less affected village. The incidence of leprosy in a group of villages, all within a radius of five miles, varied from nil to 124 per thousand. The village with the highest incidence (124 lepers per 1,000) has a village 3 furlongs away with no leprosy. Another village with an incidence of leprosy of 43.8 per 1,000, has a village less than 30 yards away with no leprosy, although the inhabitants of the latter village work in the village with leprosy. This work stresses the fact that the greatest factor in the introduction and maintenance of leprosy is contact with open cases. Proximity of an infected village, poor economic conditions, or predisposing diseases seem to play little or no part in the spread of leprosy.

Clinical studies have been concerned with the correlation of the clinical signs with the changes in the skin and other tissues produced by the leprosy bacilli. Therapeutic experiments on the trial of new remedies have so far given inconclusive results. Studies to indicate more clearly the best dosage of hydnocarpus remedies showed that a combination of intradermal and subcutaneous injections appeared to be the best. There seemed to be no advantage in giving a very high dosage. Studies of the Wassermann test in leprosy and its response to treatment indicate that the leprosy itself and not syphilis was frequently the cause of the positive Wassermann and Kahn tests.

PLAGUE

(1) At the Haffkine Institute, Bombay, the value of sulphathiazole and sulphadiazine was assessed in a trial carried out at Poona. Cases of bubonic plague treated with sulphathiazole had a mortality of 21.3 per cent, cases treated with sulphadiazine a mortality of 12.3 per cent whereas control cases—given the usual hospital treatment, i.e. iodine injected into the blood—had a mortality of 53.6 per cent. The results of the treatment in septicæmic cases was even more striking; the mortality in sulphathiazole series was 37.5 per cent, in sulphadiazine series 20.9 per cent and in the controls 91.0 per cent. No serious ill effects were encountered in cases treated with either of the two drugs (this is a very real advance in the treatment of this much dreaded disease).

A new plague vaccine has been prepared in a new broth medium. The protective power (in animal experiments) of this vaccine was twice as great as the

original Haffkine vaccine and slightly more than agar vaccine. Its toxicity was low and keeping properties better than the phenol preserved agar vaccine.

(2) The Plague Inquiry in the Salem District, Madras, studied the prevailing rodents and their fleas contributing to the endemicity of bubonic plague. The 'flea index' for different species of rat fleas was worked out. A study of rodent nests was made and the fleas in them identified and in this way the preferential environmental conditions favouring the numerical prevalence of the respective fleas established. In addition to this rodent and flea survey, vigorous cyanogas fumigation was carried out in all the villages in the experimental areas. There was noticeable reduction in the incidence of plague in spite of the somewhat restricted application of cyanogas due to restricted supplies. Five hundred and sixty-four cases were treated with sulphathiazole and allied groups of drugs. Of these, 194 cases were treated with sulphathiazole with a mortality of 29 per cent.

PHARMACOLOGY

(1) Indigenous Drugs Inquiry at the School of Tropical Medicine, Calcutta. A miscellaneous group of 10 indigenous drugs were tested for their active principles and their properties recorded. Of them two were of particular value and interest, *Daemia extensa*, a plant known as 'chagalbanti' in Bengal and a reputed drug in the indigenous system was found to contain a substance which has the properties of raising blood pressure and contracting the uterus of animals. The other drug that has been studied extensively is *Rauwolfia serpentina*, one of the active principles of which has the opposite effect to the above drug. The active principles have been isolated—the blood pressure lowering principle is an alkaloid and the hypnotic principle is contained in the resin. A study of the amount of the resin in this plant growing in different parts of India was made and the resin content was found to vary between 1.14 to 1.8 per cent. In addition five drugs claimed to be anti-malaria remedies were tried in malaria cases. None of these was of any definite value.

The Indigenous Drugs Inquiry at the Drug Research Laboratory, Jammu (Kashmir), recorded the chemistry and pharmacological action of a number of indigenous drugs. The effect of drying pyrethrum under different conditions was studied. The highest yield of pyrethrum was from flowers dried partly in the sun and partly in the shade. A number of essential oil bearing plants growing wild in Kashmir State were examined for their essential oil content. Work on the distribution of medicinal plants in India is also being carried out.

Pharmacological Inquiry at the Haffkine Institute, Bombay, investigated three new synthetic anti-malarial drugs in rhesus monkeys injected with *Plasmodium knowlesi*. All the three drugs showed anti-malarial property but in all three this property was inferior to that of sulphathiazole administered similarly and in comparable doses. Experiments in immunity in monkey malaria were also carried out. By replacing to a large extent (about 80 per cent) the blood of an immune large size monkey with the blood of an ordinary monkey susceptible to monkey malaria and then immediately infecting this large sized monkey with malaria parasites, a typical fatal malaria attack was produced. This experiment showed that the immunity in the large size monkey was 'cellular' and not 'humoral'. This inquiry was closed in October 1944.

OTHER RESEARCHES

The Hæmatological Unit at the School of Tropical Medicine, Calcutta, studied methods of preventing malaria which is sometimes transmitted by infected donor blood in blood transfusions. Stored blood containing malaria parasites when treated with quinine in concentration of 1 in 500 did not infect monkeys and experiments with weaker dilutions of quinine are in progress.

The effect of M&B 693 on the blood-forming system of monkeys was studied. With heavy doses of this

drug some deaths occurred and the blood-forming system was affected. Different monkeys varied, however, in their reaction to this drug, but in the same monkey the action depended on the concentration of the drug in the monkey's blood. An attempt was made to study anaemia in monkeys produced by injections of arsphenamine (in doses sufficient to cause liver damage) as has been done in dogs, but the arsphenamine did not produce anaemia in the experimental animals.

The Inquiry into Medical Mycology at the School of Tropical Medicine, Calcutta, studied 983 cases of ringworm infection of the body, of the nails, toes and inter-digital spaces and of the hair. Racial and seasonal occurrence of these conditions was studied and also the causative organisms. The fungicidal action of various agents was tested and in clinical trials of 2 per cent solution of glacial acetic acid in 25 per cent alcohol gave the best results; it is fairly reliable as a prophylactic against ringworm infection if used regularly during the hot weather and the monsoon months, when the incidence of ringworm infection is the highest. This preparation is not irritant to the skin, non-corrosive and non-staining.

Studies in tests of physical fitness in Indians at the Grant Medical College, Bombay.—The Crompton test was carried out on 495 subjects, 418 males and 77 females. The males and females were arranged in three groups: 'no exercise', 'moderate exercise', and 'athletic'. There were no females in the athletic group. The mean scores of fitness (Crompton scale) was 'no exercise'—males 77, females 68; 'moderate exercise'—male 73, females 75; 'athletic group'—males 78. The influence of exercise, sex, diet and community on the results obtained led to the conclusion that the Crompton test is not as good a test for grading physical fitness of an individual as the Schneider test.

Filaria Inquiry at the School of Tropical Medicine, Calcutta, carried out field studies in Bengal and in the Central Provinces of the incidence of filarial infection and of the vector mosquito. Most filarial infections were due to *Wuchereria bancrofti* but in one area *W. malayi* was found. Studies of the periodicity of the microfilaria have been carried out and several different drugs including some of the indigenous remedies and some synthetic compounds have been tested in the treatment of filarial infection, all with unsatisfactory or inconclusive results.

Inquiry on Filtrable Viruses at the King Institute, Guindy, studied the relative value of smallpox vaccine grown on chick membrane and the usual calf lymph smallpox vaccine in the prevention of smallpox, the production of agglutination of red cells by chick membrane vaccinia virus. Attempts were made to adapt a mouse strain of virus to eggs without success; also to isolate the virus of anterior poliomyelitis and of infective hepatitis.

Kala-azar Inquiry at the Pasteur Institute, Shillong, carried out seven experiments to infect white mice with sandflies fed on kala-azar cases; in one of the 7 animals infection took place and the infecting organism of kala-azar was demonstrated in the spleen of the mouse. A study of the longevity of sandflies maintained under different conditions of blood feeds, temperature and humidity shows that there is no hibernation in the strict sense but with the lowering of temperature, the development stages are prolonged to double the time taken in the incubator, thus explaining the small catches of adults in the cold months. For this work 24,141 sandflies were bred in the laboratory; the reaction of the gut of these flies was estimated by a delicate method and found to be 7.2 to 7.6, i.e. slightly alkaline.

The inquiry on anaerobic wound infections at the Seth G. S. Medical College, Bombay, carried out laboratory studies of toxin and enzyme production, haemolytic activity, spreading factor and serological reactions of 19 strains of organisms causing gas gangrene.

The inquiry into methods for the manufacture of solid blood plasma, etc., at the All-India Institute of Hygiene and Public Health, Calcutta, tried out methods

for improvements in pooling, filtration, storage and processing of dried serum. The total number of batches dried was 61 comprising 3,598 bottles and 1,439.2 litres of serum, and 4,675 liquid and 2,037 dried sera were issued.

The inquiry into the occurrence of ascites in Hyderabad State, at the Osmania Medical College, Hyderabad, Deccan, carried out a preliminary survey. Of the 343 cases of ascites admitted to hospital, 37 per cent were associated with damage to the liver, 15 per cent with heart disease, 11 per cent with kidney disease, 10 per cent with tuberculosis and 6.4 per cent with malignant disease. In 15 per cent no obvious cause was found for the ascites; a majority of these were cured or much improved after rest and a liberal diet. These latter were considered as nutritional deficiency ascites.

The inquiry on the action of snake venoms and their constituents on the biochemical activity of the tissue cells at the University College of Science and Technology, Calcutta, investigated the following points: (i) the inhibition of certain enzyme activities by cobra venom, (ii) the isolation (by fractional precipitation) of a toxin in cobra venom which stops the movement of the heart, (iii) the inhibition by cobra venom of the synthesis of acetylcholine, and (iv) the isolation of the active principle in cobra venom which inhibits glycolysis.

The inquiry on typhus at the Haffkine Institute, Bombay.—In collaboration with the military authorities strains of XK typhus organisms were isolated using white mouse for the isolation and maintenance of these strains. Duck eggs were used for the cultivation of the causative organisms. With the strains isolated batches of mice were infected and representative compounds (synthesized at the Institute) of the sulphonamide group of drugs tried in the treatment of the experimental infection. None of the drugs tested had any therapeutic value. An analysis of symptoms of typhus cases occurring in Bombay was made. Of the 63 cases, 47 were among Indians and 16 among Europeans. The average duration of fever among the Indians was 13.5 days and among the Europeans 15.5 days. Rash was present in 13 cases, 10 being Indians and 3 Europeans. There was only one death, 1.6 per cent. One strain of typhus X19 in type was isolated in Bombay. The relation between this strain and similar strains from U.S.A. was examined by animal experiments. The typhus strain of Bombay is much less virulent than the American strain. Improvements in the methods of diagnosis have been worked out and a method of rapid bedside diagnosis introduced. Typhus in Kashmir was studied. The positive Weil-Felix reactions in pregnancy and cancer reported in recent medical literature was not confirmed by tests carried out in Bombay.

The inquiry into vaccine lymph, at the Department of Public Health, Bombay, examined methods of reducing the bacterial content in smallpox calf lymph vaccine. Various purifying agents in different concentrations were used. The results show that the usual method of purifying by using glycerine and chloroforming the best. Data were also collected as to the average duration of immunity after successful vaccination with smallpox vaccine lymph, with less than 5 years' interval between vaccinations all individuals show full or partial immunity, with intervals of 6 to 10 years 76.9 per cent are immune or partially immune, and 23.1 per cent are susceptible.

The inquiry into Naga Sore, Shillong, carried out a preliminary survey of the incidence of these chronic debilitating ulcers and made plans for future work.

The inquiry into the fraction of the liver most suitable for the treatment of tropical macrocytic anaemia at the School of Tropical Medicine, Calcutta, has carried out some studies of different Cohn fractions of liver in the treatment of tropical macrocytic anaemia.

The inquiry on schistosomiasis in the Army, at the School of Tropical Medicine, Calcutta, made some attempts to infect Indian snails with *Schistosoma mansoni* in the laboratory but without success.

Correspondence

BLOOD STAINING FOR MALARIA PARASITES

SIR,—The methods of staining blood films described by Field and Simeons take only a few minutes time, but the actual process of staining requires a series of immersions and rinsings in stains and water respectively. Also the correct preparation of stains as described by them (Field and Simeons) may not be possible in tea garden hospitals except where there are elaborate laboratory arrangements. As a tea garden practitioner, I still find the following two methods easy and of value. These are Sinton's methods with a slight modification:

(A) Combined thick and thin film staining: Two drops of blood are taken near one end of a slide. The drop nearer the end of the slide is spread into a circle as a thick film (not too thick), the other drop is spread into a thin film towards the opposite end of the slide. The two films are separated by a line drawn by a grease pencil. Romanowsky stain is poured on the thin film; after a minute dilute Giemsa's stain (one drop of Giemsa's stain to 1 c.cm. of distilled water) is poured on it. Now the mixture of Romanowsky and dilute Giemsa's stain is drawn on to the thick film across the grease pencil line with a needle, the slide is washed after 10 minutes and is ready for use within 15 minutes. A number of slides can be stained at one time by this method.

(B) A thick drop is taken and dried. The dilute Giemsa's stain is poured on it and washed after half an hour. A large number of slides can be stained at one time.

In the thick films stained by the above two methods, the red cells do not show, the leucocytes are stained well, the malaria parasites are well stained, and the type of infection also can be determined with accuracy. The method 'A' is followed in special cases where immediate diagnosis is necessary, e.g. cerebral or algid cases, or where study of the red cell condition is necessary, or where the type of infection is to be decided. Diagnosis is made by first examining the thick film and then the slide is moved and the thin film studied. But as a routine procedure in hospital admissions the 'B' method is followed.

In busy seasons thick drops from 2 or 3 patients are taken on one slide and numbered and stained.

In this method there is economy in the use of slides, in stain and in time. I use Giemsa's stain from Messrs. Bathgate and Co., with satisfactory result.

R. K. DE.

TALUP TEA ESTATE,
UPPER ASSAM.

WEIGHT, HEIGHT AND CHEST MEASUREMENTS IN THE CLASSIFICATION OF TYPES OF INDIVIDUALS

SIR,—I was interested to read in your June number the article by Mr. M. G. Kini regarding 'Weight, height and chest measurements in the classification of types of individuals', page 301.

The French have a system called 'Pignet' from the name of the inventor, by which a man's weight in kilograms added to the chest circumference in centimetres should be as near as possible to his height in centimetres.

For instance, a man like myself measuring 95 cms. around the chest, weighing 65 kilos and being 163 cms. tall has a 'Pignet' of -3, this being the difference between the two sets of figures:

$$95 + 65 = 160 - 163 = -3.$$

The French army has a classification by groups according to the Pignet being - or + and by difference of 10, if I remember right. People within the first group -10 or +10 are good and the rest proportionately are bad. You could certainly get the correct

information from the Service de Sante of Pondicherry, where the system is employed regularly for the police recruitment by instance, and your readers would certainly be interested in having more details about the system.

P. PAGNON,
Manager.

PACIMEX COMPANY,
RAHIMTOOLA HOUSE,
HOMJI STREET, FORT,
BOMBAY,
19th September, 1945.

TREATMENT OF CEREBRO-SPINAL FEVER WITH SULPHAPYRIDINE

(A SUGGESTION)

SIR,—With reference to the article on 'Treatment of cerebro-spinal fever with sulphapyridine', published in your June issue of the *Gazette*, conclusion para 5.

It has been emphasized in the article that eight pints of 5 per cent glucose solution should be administered orally in the twenty-four hours. Is there any special reason why only this solution should be given?

A well balanced, nutritious, fluid intake, including sufficient alkalies to keep the urine on the alkaline side, should be more beneficial to the patient, if it is administered by a transnasal intragastric Ryles' tube, which may be left in for a considerable period and the patient nursed in the sitting posture to ensure effective reduction in the intracranial fluid tension.

M. TAJUDDIN,
CAPTAIN, I.M.S./I.A.M.C.

COMBINED SERVICES HOSPITAL,
CEYLON,
16th September, 1945.

PALUDRINE—M.4888

[The following are extracts from a letter received from the Imperial Chemical (Pharmaceuticals) Ltd., Manchester. See editorial note on page 513.]

SIR,—You will perhaps know that the Liverpool School of Tropical Medicine have announced the discovery of M.4888 as an antimalarial drug.

In view of the urgency of applying a proper name to this drug we decided to use the name 'Paludrine' in spite of the fact that this name had previously been applied to M.3349. We were under the impression that the name had not been mentioned in print because of the secrecy regulations governing all antimalarial research. I am afraid we did not know of your paper in the *Indian Medical Gazette* of May 1945.

There is no doubt that the conclusions at which you arrive in that paper suggest that M.3349 is unsuitable as an antimalarial drug. There is equally no doubt that M.4888 is vastly superior to it.

We should be very obliged, therefore, if you could assist us in transferring the name 'Paludrine' from M.3349 to M.4888 by a short announcement in your journal.

C. M. SCOTT,

IMPERIAL CHEMICAL (PHARMACEUTICALS), LTD.,
HEXAGON HOUSE, BLACKLEY,
MANCHESTER, 9.

Service Notes

APPOINTMENTS AND TRANSFERS

COLONEL K. S. MASTER, M.C., is appointed Honorary Physician to the King, with effect from the 30th July, 1944, *vice* Colonel A. C. Macrae retired.

Colonel W. C. Spackman, V.H.S., is appointed Honorary Surgeon to the King, with effect from 31st

October, 1944, *vice* Major-General Candy, C.I.E., retired. The services of Lieutenant-Colonel I. S. Nalwa, are placed at the disposal of the Government of Bihar for employment in the Jails Department, with effect from the 19th April, 1943.

In exercise of the powers conferred by sub-section (i) of 3 and 6 of the Indian Emigration Act, 1922, the Central Government is pleased to appoint Lieutenant-Colonel E. Montgomery, Civil Surgeon, 24-Parganas, Bengal, as the Protector of Emigrants, and the Medical Inspector of Emigrants, Calcutta, with effect from the forenoon of the 1st August, 1945, *vice* Lieutenant-Colonel R. A. Wesson, granted leave.

Lieutenant-Colonel L. E. Gilbert, a retired officer of the Indian Medical Service, is appointed as officer on special duty in the Commonwealth Relations Department, with effect from the 6th August, 1945, until further orders.

Lieutenant-Colonel W. H. Crichton, C.I.E., on reversion to the civil employment has been appointed as Director of Public Health, C. P. and Berar, and he assumed charge on the forenoon of 20th August, 1945.

Lieutenant-Colonel W. Scott, Civil Surgeon and Superintendent, Robertson Medical School, Nagpur, has been appointed to officiate as Inspector-General of Civil Hospitals, C. P. and Berar, with effect from 22nd August, 1945, *vice* Colonel A. H. Harty, C.I.E., granted leave.

The services of Major J. H. Gorman are placed at the disposal of the Government of Madras, with effect from the afternoon of the 15th February, 1945, for appointment as Director of Public Health, Madras.

Major C. Mani is appointed. Additional Deputy Public Health Commissioner with the Government of India, with effect from the 18th July, 1945.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commission)

The undermentioned officer is transferred to the general service cadre with effect from the date specified :—

Captain Husain Reza. Dated 27th June, 1945.

INDIAN MEDICAL SERVICE—SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

To be Captains

(Miss) Ruby Vurgese. Dated 16th February, 1945.

Shankar Anant Ajaonkar. Dated 15th April, 1945.

Krishna Kumar Gupta. Dated 20th May, 1945.

To be Lieutenants

Pallassena Pachveetil Sadasiva Menon. Dated 2nd May, 1945.

Mahboobuddin Siddiqui. Dated 14th May, 1945.

Bolar Shivshanker. Dated 15th May, 1945.

Kshetra Mohon Banik. Dated 18th May, 1945.

Panikulam George Paul. Dated 18th May, 1945.

19th May, 1945

Venkatarama Ranganathan, Sivasubramanian Thirumalai, Nagarur Gopinath, Thillaigovindan Ramaswamy, Nalapat Kesava Menon, Poluvan Krishniya Srinivasan.

20th May, 1945

Danasamy Joseph Antony, K. V. Menon, Krishna-swamy Mahadeva Iyer, Bale Bail Krishnachar, Makkuni Narayanan Nambiar.

Dhadeshwar Ramesh Rao. Dated 21st May, 1945.

The undermentioned officer of the I.M.S. (E.C.) reverts from the R.I.N.V.R. and is seconded to the I.A.M.C.:—

Surgeon-Lieutenant Krishan Kumar. Dated 15th May, 1945.

LEAVE

Major M. Sendak, O.B.E., Officer on Special Duty, Home Department, is granted leave for 6 months, with effect from 9th June, 1945.

PROMOTIONS

Lieutenant-Colonels to be Colonels

P. H. S. Smith, O.B.E. Dated 31st October, 1944.

T. R. Khanna. Dated 17th April, 1945.

INDIAN MEDICAL SERVICE—SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(WOMEN'S BRANCH)

(Emergency Commissions)

Lieutenants to be Captains

26th October, 1944

Mrs. B. N. Akeroyd. Miss K. M. Blacklock.

RETIREMENTS

Colonel R. V. Martin, C.I.E. Dated 13th July, 1944.

Major-General R. H. Candy, C.I.E. Dated 1st January, 1945.

RELINQUISHMENTS

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Major S. A. De Souza, 2nd June, 1945, on grounds of ill health and is granted the honorary rank of Major.

Major W. M. D'Souza, 20th July, 1945, on grounds of ill health and is granted the honorary rank of Major.

Captain Sailendra Prasad Mitra, 22nd July, 1945.

Captain (Miss) Leela D. Tilak, 24th July, 1945, on grounds of ill health and is granted the honorary rank of Captain.

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Original Articles

CARCINOMA OF THE APEX OF THE LUNG WITH HORNER'S SYNDROME*

By P. V. GHARPURE

MAJOR, I.M.S./I.A.M.C.

CASES of tumours situated in the apex of the lung with a certain group of signs and symptoms described as Horner's syndrome have been published in the literature since Pancoast (1924) first described three cases of apical lung tumours. Pancoast (1932) again described four more such cases and gave them the name of 'superior pulmonary sulcus tumour'. In none of his cases were autopsies performed, and in only two cases were biopsies done. Pancoast advanced the idea that perhaps these tumours might have arisen from embryonic branchiogenic rests and that he was dealing with a new type of apical lung tumour. Pancoast was aware that his cases were incompletely studied, and wisely concluded that additional knowledge from a more thorough study of other cases might make it necessary to abolish the term 'superior pulmonary sulcus tumour' as implying a specific tumour in the apex. Browder and DeVeer in 1935 described five cases and reviewed the literature on this subject, and arrived at the conclusion that the symptom complex of a superior pulmonary sulcus tumour did not represent either a clinical or a pathological entity among tumours. Hall in 1940 reviewed the literature on this subject and described five cases of his own. He concluded from the reported cases that most apical tumours are primary in the lung, but that other primary tumours, as well as metastatic tumours, occur in this region, and that any of them can simulate the tumours described by Pancoast. Monteiro (1943) reported a case of bronchogenic squamous carcinoma of the right apex with Horner's syndrome in a male aged 40 years. A complete autopsy was done on this case. Athle in 1944 has briefly discussed the pertinent facts about the Pancoast syndrome, and has referred to seven cases studied by him of apical lung tumours with Horner's syndrome. In one case a lobectomy was done and the pathological report was a bronchogenic squamous carcinoma. In the rest of the six cases, aspiration biopsy was done and the pathologist reported a malignant tumour. The origin and exact nature of these cases could not be determined further.

The following case of a primary adenocarcinoma at the apex of the lung with Horner's syndrome was studied in detail, including an autopsy.

Brief case report.—A European male, aged 39, was admitted to the hospital on 18th March, 1945. He complained of pain on the right side of the chest, in the right shoulder and the inner side of his right forearm. He also complained of generalized pain in all his bones. *Previous medical history:* A history of a sore on the penis for which he received adequate anti-syphilitic treatment in 1936; a complaint of pain in the extremities in February 1944. Knee and ankle joints had been swollen and contained fluid, and there was cough with breathlessness. He had been given a course of sulphathiazole (54 gm. over 8 days) without benefit. He was again given antisyphilitic treatment. Later (16th December, 1944), he noticed enlargement of the ends of long bones and clubbing of the fingers, muscle wasting and œdema of the extremities. Blood studies showed a macrocytic anæmia but a normal total and differential white cell count. Blood sedimentation rate 100 mm. after one hour. *X-ray report* (4th June, 1944): Long bones showed evidence of periostitis. *Chest:* Signs of chronic bronchitis. Left cervical rib seen. On 21st November, 1944, increased opacity in the region of the right apex was seen. In December 1944, he was noticed to be developing a syndrome of collapse of the right lung with myosis of the right eye and pain in the radicular distribution of the roots of C 8, T 1 and T 2. A diagnosis of generalized periostitis and gumma of the right upper lobe of the lung was thought of. He was given penicillin, but with no benefit. His general condition gradually deteriorated, with a loss of 30 lb. weight in the last two months. Finally a diagnosis of Pancoast tumour was made.

On examination (26th March, 1945)—*Eyes:* Mucopurulent discharge; *Pupils:* Right contracted, both react to light briskly. *Chest:* Hollowing and diminished movement above and below the right clavicle. Percussion note dull; fine crepitant râles. Posteriorly, slight wasting of right supra- and infra-spinatus muscles; percussion note impaired in upper and middle zones; breath sounds harsh and vesicular, with a cavernous quality opposite the third vertebra. *Heart:* Nothing abnormal detected. *Limbs:* Marked clubbing of the fingers and toes. Thickening of bones of the limbs. *C. N. S.:* Nothing abnormal detected. *Clinical diagnosis:* Pancoast tumour with a severe degree of hypertrophic pulmonary osteoarthropathy. Erosion of the second and third ribs by the tumour. He was given a course of deep x-ray therapy, 2,000 roentgen units in 10 days. His general condition gradually became worse and he died.

Significant post-mortem findings (30th May, 1945): A large tumour mass was situated in the right upper lobe (figure 1, plate XX). The

* Horner's symptom complex is defined by Stedman's Medical Dictionary as follows: Ptosis, myosis, anidrosis and enophthalmos due to paralysis of the cervical sympathetic.—EDITOR, I.M.G.

cut surface of the tumour showed areas of marked softening and necrosis (figure 2, plate XX), and on squeezing a purulent fluid oozed out. The main bronchi were cut open, but the tumour had apparently no connection with them. The tumour had eroded the first, second and the third right ribs and caused pathological fractures of the first and second ribs. The tumour had infiltrated the bodies of the sixth and seventh cervical vertebrae. *Brain*: In the floor of the right lateral ventricle a small cellular growth, 2 cm. in diameter, was seen bulging into the anterior horn. The rest of the organs in the body were carefully examined for gross lesions, but there were no pathological findings of significance. *Histological examinations*: (1) Section of the tumour from the lung showed large irregular groups of large atypical polygonal and columnar cells. They are separated by a connective tissue stroma. The cells have very irregular shapes and sizes. The cytoplasm is acidophilic. The nuclei are round and ovoid, and vary in size and shape. Tumour giant cells with multiple round and ovoid hyperchromatic nuclei are seen. There are areas showing a definite acinar arrangement of the cells. The tumour shows areas of marked necrosis and degeneration. The stroma contains a few thin-walled blood capillaries. Tumour emboli are found in blood vessels. *Diagnosis*: Adenocarcinoma grade II (figure 3, plate XX). (2) A section of the brain metastasis showed a histology similar to that of the primary in the lung. (3) A section of the adrenal did not show tumour deposits.

Summary.—This patient had a primary carcinoma of the right upper lobe of the lung with a small metastasis in the brain. There was erosion of the first, second and third right ribs and bodies of the sixth and seventh cervical vertebrae. He had pain and wasting of the muscles of the chest and of the right superior extremity. There was myosis of the right eye.

Conclusion.—A thoroughly studied case of primary bronchogenic adenocarcinoma of the right upper lobe of the lung with the symptom complex described as Horner's syndrome is reported. There was no evidence to support the idea of a superior pulmonary sulcus tumour being a tumour entity by itself, as originally described by Pancoast.

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PENICILLIN IN CANCRUM ORIS COMPLICATING KALA-AZAR*

By P. C. SEN GUPTA, M.B. (Cal.)

and

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CANCNUM oris is the most classical and the most fatal complication of kala-azar. Previous to the introduction of the specific treatment with the antimonials, cancrum oris was the terminal event in a large proportion of cases. The incidence of this fatal complication decreased very considerably with the adoption of the specific treatment with the antimonials during the last twenty-five years or so. But during the last three years, particularly during and after the famine of 1943, the senior writer has come across an increasingly large number of cases of kala-azar complicated with cancrum oris; the results of treatment could by no means be regarded as satisfactory, about half the cases admitted to hospital dying.

The treatment adopted was that which had developed during the last 20 to 25 years as a result of treatment of numerous cases in India and abroad. It consisted of: (a) intensive specific treatment with pentavalent antimony compounds, the injections being given daily; (b) general treatment designed (i) to raise the body resistance, viz, adequate nourishment, vitamin intake, blood transfusions, (ii) to combat the infection, viz, sulphonamides (various vaccines and antisera have been abandoned during recent years), intravenous injections of arsenicals in case of Vincent's infections, etc., (iii) to raise the leucocyte count by the injections of pentnucleotide or liver extract; and (c) local treatment generally by mild antiseptics. In some cases sulphonamides were applied locally.

In spite of all these therapeutic measures, the condition was very often fatal. Death was usually due to the spread of infection intracranially, aspiration broncho-pneumonia, obstinate diarrhoea, and asthenia and cachexia due to septic absorption. Sudden death within 12 to 24 hours of admission into the hospital, possibly due to intracranial extension of infection, was also seen. In some cases, the specific and other therapeutic measures did not check the process at all. The worst case the senior writer has seen was in a boy in whom the gangrene spread relentlessly day by day from a small necrosed area in the left cheek to the mandible, left maxilla, left eye, left temporal region, left ear, nose and part of the frontal bone, in spite of the entire regime of treatment.

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enumerated above; ultimately the fatal termination ended the misery of the patient who was conscious almost to the end.

The usual course of the cases that responded to treatment was that for some days the necrotic process kept on spreading to the adjoining tissues; then a line of demarcation formed, and the slough slowly separated leaving a hideous deformity that slowly healed at the margins by granulation. Figures showing the actual proportion of cases that recovered in India are not definitely known. In China where about 15 per cent of kala-azar cases were found to develop cancrum oris, Fu-tang Chu and Chuan Fan (1936) found that 39 out of 79 cases died (about 50 per cent), and in children below 2 years 77.7 per cent cases died.

With the introduction of penicillin and its reported success in the treatment of wound infections about the mouth, it was felt that this drug might prove successful in the treatment of the infective process of cancrum oris. Six cases of cancrum oris coming under treatment between March and September 1945 were treated with penicillin along with the specific anti-kala-azar treatment and general supportive measures. The reports of these six cases are presented below:

Case 1.—An Indian child, aged 5 years, was admitted on the 19th March, 1945, for fever, irregular and intermittent in type, for three months, and ulceration of the upper lip and root of the nose for about 1 month. She had been treated outside with some intramuscular injections of antimonials. On admission the child was found to be extremely anæmic and emaciated with a temperature of 102°F.; the spleen was enlarged up to 1½ inches below the tip of the 9th left costal cartilage; the liver was palpable; in the heart and lungs no abnormality was detected. There was a foul-smelling black gangrenous ulceration involving the upper lip, left cheek, root of the nose and a part of the nasal septum (see figure 1, plate XX).

Laboratory findings were as follows: Hb.—4.8 gm. per 100 c.c. of blood; RBC—2,010,000/c.mm.; WBC—5,700/c.mm.; neutrophils—42 per cent; lymphocytes—37.5 per cent; monocytes—19.5 per cent; Türk cells and plasma cells—1 per cent. Antimony test (1:10)—positive; complement-fixation test for kala-azar—doubtful. Stools showed ascaris ova, 1,000/c.c.; pus from the cancrum area showed gram-positive cocci in clusters and chains and fusiform bacilli.

She was put on penicillin and urea stibamine immediately on admission. Penicillin was administered intravenously in 10,000-unit doses every three hours for 6 days, and applied locally in a solution containing 500 units per c.c. for about a fortnight. Urea stibamine was given on consecutive days for ten days and then on alternate days till the 19th injection (total dose 2.3 gm.).

Within 24 hours of the commencement of the treatment, the slough appeared to be getting loose and by 48 hours the slough separated, leaving a clean granulating margin; the foul smell had practically disappeared and the fever had also subsided. The patient progressed steadily except for a slight set-back following an attack of common cold when she required a second course of penicillin in order to check a threatened spread to the nasal septum. The subsequent recovery was uneventful. The patient was discharged on the 16th May with a clean and healed sore (see figure 2, plate XX).

The blood count on discharge was as follows: Hb.—9.07 gm. per cent; RBC—3,650,000/c.mm.; WBC—

5,400/c.mm. She was advised to attend the surgical division of the Medical College Hospital, Calcutta, for a plastic operation.

Case 2.—An Indian female child, aged 2½ years, was admitted on the 16th April with a history of fever with chill and rigor for 6 months, attacks of diarrhoea for 3 months and a perforating ulcer of the cheek that had developed during the previous week or so. The child was extremely emaciated and anæmic and had an ulcer covered with slough over the right maxillary antrum. The spleen was enlarged 1 inch below the costal margin and the liver was just palpable. The heart and the lungs did not show any obvious abnormality. The temperature was subnormal.

Laboratory findings were as follows: Hb.—6.18 gm. per cent; RBC—2 million/c.mm.; WBC—7.4 thousands/c.mm.; neutrophils—46 per cent; lymphocytes—48 per cent; monocytes—6 per cent. The complement-fixation test for kala-azar was positive and tibial puncture showed numerous leishmaniae. Stools—ascaris ova 300/c.cm. and *E. nana* cysts. Urine—no abnormality.

She was put on penicillin 10,000 units intramuscularly every three hours for 8 days, and a solution containing 500 units of penicillin per c.c. was applied locally for about a fortnight. She also had specific treatment for kala-azar with urea stibamine, 0.05 gm. given intravenously for ten consecutive days and then on alternate days in 0.1 gm. doses till a total of 1.5 gm. had been given. By the 25th April she was afebrile, and the ulcer was healing, but there was a fistula opening into the mouth. As the patient was having occasional attacks of fever and the spleen was still enlarged she was given another course of twelve daily injections of aminostiburea, total dose 1.15 gm. She was discharged cured on the 19th June, 1945; she had put on 4 lb. in weight; the spleen was reducible, and the blood count showed some degree of improvement; the ulcer had healed completely leaving a small scar adherent to the maxilla, but the fistula had closed.

Case 3.—An Indian male child, aged 3 years, was admitted on the 8th June, 1945, for fever of six months' duration; it was high continuous for about 6 weeks and irregular subsequently. There was a history of occasional swelling of the feet; there was a foul-smelling ulceration over the lower lip and loss of several lower incisor teeth. This condition had developed during the previous seven days.

On admission the patient was found to be very thin and anæmic. He was having a high remittent fever, the temperature rising to 103°F. The hair was thin, dry and lustreless, and the skin showed some degree of pigmentation and dryness. There was a foul-smelling ulceration with black slough involving the lower lip with a fistula into the mouth. Some of the lower incisors were missing and the mandible was apparently affected. The spleen was enlarged (five inches) and the liver was palpable.

Laboratory findings were as follows: Hb.—4.4 gm. per cent; RBC—1.32 millions per c.mm.; WBC—4.1 thousands per c.mm.; neutrophils—52 per cent; lymphocytes—24 per cent; monocytes—20 per cent; plasma cells and Türk cells—4 per cent. The aldehyde test was positive; the complement-fixation test, doubtful. Stools—cysts of *giardia intestinalis*. Culture of swab from the cancrum showed streptococci (not hæmolytic) and *Staphylococcus aureus*.

The treatment with 'stibatin' and penicillin parenterally and locally was commenced from the day of admission. Twelve intramuscular injections of stibatin were given on consecutive days (total dose 90 c.c.). Penicillin was given as in the other two cases. Within 48 hours of the commencement of the treatment, the sore appeared cleaner; the black slough of the lower lip separated, and the foul smell diminished considerably. His general condition also improved, and the fever disappeared from the third day of treatment.

The patient required a second course of stibatin and penicillin because signs of necrosis of the mandible persisted and the clinical evidence after the first course

of treatment did not indicate a cure of kala-azar. He was discharged on the 25th July apparently cured of kala-azar with a healed ulcer on the lower lip. The necrosed bit of the mandible was loose at one end only. He was advised to attend the surgical unit of the Medical College Hospital, Calcutta.

Case 4.—An Indian female child, aged 4 years, was admitted on the 9th August, 1945, for intermittent fever with chill and rigor, slight cough, weakness and emaciation for four months. On admission the child was found to be weak, emaciated and anæmic but apyrexial. She had cancrum oris involving the whole of the inner aspect of the left cheek. The ulcer was foul smelling and covered with a greenish-yellow slough. A few small whitish patches were also present under the tongue and on the inner aspect of the lower lip. The spleen was enlarged to 2 inches and the liver was 1 inch below the costal margin.

Laboratory findings were as follows: Hb.—6.87 gm. per cent; RBC—2.41 millions per c.mm.; MCV—99.5 μ ; MCH—28.5 γ ; MCHC—28.6 per cent; WBC—3,750 per c.mm.; neutrophils—38 per cent; lymphocytes—48 per cent; monocytes—13 per cent; plasma cells—1 per cent. Aldehyde test—negative. Antimony test—doubtful. Complement-fixation test for kala-azar—negative. Tibial puncture—Leishman-Donovan bodies present. Swab from the cancrum oris—gram-positive cocci and bacilli, gram-negative bacilli, fusiform bacilli, and spirochaetes present. Stools—ova of ascaris, 5,800 per c.c.

The treatment was commenced immediately on admission, with penicillin given locally and by intramuscular injections, and daily injections of stibatin. Within 24 hours of the commencement of the treatment the cancrum appeared cleaner and the foul smell was considerably less. By the next day the smell had disappeared completely. The slough separated on the third day and by the sixth day the necrosis had stopped, and the ulcer was covered by newly-formed epithelial tissue. Her clinical condition had improved considerably and she was discharged as clinically cured of kala-azar on the 3rd September, 1945.

Case 5.—An Indian female child, aged 10 years, was admitted on the 27th August, 1945, for intermittent fever with chill and rigor and occasional bleeding from the gums for three months. On admission she was found to be anæmic and emaciated with enlarged cervical glands and oedema of the legs. The spleen was enlarged up to 3 inches and the liver was just palpable. Heart and lungs showed no abnormality. An ulcer was noticed on the left side of the hard palate affecting its anterior half. It was covered with greyish-white slough.

Laboratory findings were as follows: Hb.—6.05 gm.; WBC—2,300 per c.mm. Aldehyde test—doubtful. Complement-fixation test for kala-azar—strongly positive. Sternal puncture—Leishman-Donovan bodies present. Swab from the cancrum—fusiform bacilli, spirochaetes, gram-positive and gram-negative bacilli and cocci.

She was put on daily injections of aminostiburea, penicillin and vitamin C. Within three days the slough separated and the ulcer was free from the foul smell; by the sixth day the ulcer appeared to be healed. Her temperature came down to normal on the fifth day. She was discharged cured a month after admission.

Case 6.—An Indian male, aged 22 years, was admitted on the 8th August, 1945, for intermittent fever, occasional attacks of diarrhoea, cough and bleeding from the gums for 3 months, and ulceration inside the mouth for ten days. On admission the patient was found to be extremely emaciated and anæmic, and in a very low condition. He had oedema of the feet and legs, and purpuric spots over the chest; the gums were spongy and bleeding. Three teeth, the upper incisors and the canine, on the right side were missing, and there was a foul-smelling gangrenous ulcer covered with a greyish slough extending over the whole of the right half of the hard palate, and the soft palate showed a large perforation with a sloughing margin.

The inflammatory process extended upwards into the nasal sinuses. The liver and the spleen were just palpable; a hæmic murmur was audible over the heart; no other abnormality was detected.

Laboratory findings were as follows: Hb.—5.2 gm. per cent; RBC—1.6 million per c.mm.; MCV—118.7 μ ; MCH—32.7 γ ; MCHC—27.5 per cent; WBC—2,500/c.mm.; neutrophils—65 per cent; lymphocytes—29 per cent; monocytes—5 per cent; plasma cells—1 per cent. Aldehyde test—negative. Complement-fixation test—strongly positive. Wassermann test—negative. Sternal puncture—Leishman-Donovan bodies + +. Swab from the cancrum—gram-positive cocci, gram-negative bacilli, fusiform bacilli and spirochaetes.

The patient was put on daily injections of aminostiburea, and on penicillin, 20,000 units given intramuscularly every three hours for ten days; penicillin was also applied locally as a spray, and by means of penicillin lozenges kept in contact with the ulcer almost continuously; supportive treatment consisting of glucose intravenously, vitamins B and C and calcium, etc., was given.

By the fourth day from the commencement of the treatment, the foul smell disappeared and the ulcer appeared cleaner. Part of the slough separated, and the margins became more well-defined. His general condition improved to some extent but the anæmia persisted. He was given a blood transfusion of 400 c.c. on the 23rd August, 1945. About three weeks after his admission, the inflammatory process again became active and spread into the orbital cellular tissue of the right side. There was a swelling of the right side of the face and over the eyelids, but there was no rise of temperature. A second course of penicillin was given. The spread of inflammation was checked and an abscess pointed below the right lower eyelid. It was drained by an incision; the pus, on examination of a direct smear, showed gram-positive cocci in clusters and short chains and fusiform bacilli.

At the end of the treatment with penicillin, it was found that the right half of the hard palate was necrosed, and the margins of the perforation of the palate were quite clean, showing granulation tissue. A second blood transfusion was given on the 21st September. On the 28th September it was found that the sequestrum had separated out. Blood tests and clinical features showed that the patient had recovered from kala-azar. The final blood count (3rd October, 1945) was as follows: Hb.—11 gm. per cent; RBC—3,430,000 per c.mm.; WBC—9,800 per c.mm.; neutrophils—72 per cent; lymphocytes—18 per cent; monocytes—7 per cent; eosinophils—3 per cent.

Discussion

It will be noted that of the six patients, 5 were children between 2 and 10 years of age and one a young adult, and the duration of illness prior to the development of cancrum oris varied from three to six months. The necrotic process had developed before the patients were admitted into the hospital, and in one case it had developed during a course of specific treatment for kala-azar.

The diagnosis of kala-azar was confirmed by the demonstration of the parasite in four cases. In the other two cases no attempt was made to demonstrate the parasite, the patients being put on specific treatment immediately on admission. In one of these patients who had a small splenic enlargement, the antimony test using the serum dilution of 1 : 10 was positive; in the other the aldehyde test was positive. The complement-fixation test was positive in three cases only. Though the number of cases is small, it appears that the proportion of positive results

(3 out of 6) is lower in these cases complicated with cancrum oris than in kala-azar cases in general, viz, 93 per cent (Sen Gupta, 1944).

The course of treatment followed in these cases was as follows: (1) Penicillin sodium 10,000 to 20,000 units given intramuscularly or intravenously every three hours for about a week and repeated if required. Local application of penicillin solution containing 500 units per c.c. and as a lozenge in one case, continued for two to three weeks. (2) Specific treatment for kala-azar with pentavalent antimonials, urea stibamine or stibatin, the injections being given daily. (3) General supportive measures, consisting of nourishing diet, vitamins, glucose parenterally, and blood transfusion and hæmatics later if required.

The progress of the necrotic process was found to be quite unlike that seen in the cases that recovered in the previous years. The necrotic process did not continue to extend into the surrounding tissues; in all but one case, the slough separated within 72 hours of the commencement of penicillin therapy; the foul smell distinctly lessened within 48 hours, and was completely absent after 72 hours. The fever commenced coming down after 24 hours and reached normal within the next few days. Apart from the fact that all the patients recovered, the end results of cancrum were fairly satisfactory.

In addition to the above cases, two more kala-azar cases with sloughing of the gum over the third molar and the mucous membrane around it were treated with penicillin, intramuscularly and locally in one, and only locally with penicillin lozenges in the other, with entirely satisfactory results. The yellowish-white slough over the affected areas cleared up readily without extension to the adjoining tissues.

It is not possible to arrive at any statistically sound conclusions about the value of this regime of treatment on the experience of such a small number of cases; but the success that attended this treatment and the marked difference in the course of the necrotic process from that experienced in the past leads the writers to consider that this regime of treatment—penicillin, pentavalent antimonials, and general supportive measures—is likely to meet with better success than the previously adopted method of treatment.

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A CASE OF MULTIPLE PRIMARY CARCINOMATA

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Mackee and Cipollaro in their exhaustive monograph 'Cutaneous Cancer and Precancer'

have given a list of causes as precancerous conditions. They say 'many if not most cutaneous cancers develop in a long-standing antecedent, recognizable lesion'. The following case is of interest in that no antecedent lesion can be held responsible for the development of malignant lesions. This patient had several intravenous injections twenty years ago. Even if one assumes these to have been of some arsenical preparation, yet there was no sign of arsenical dermatitis or keratosis, and the malignant lesions were far removed from the palms and soles. While discussing senile keratosis they say 'recent experiments on albino animals have shown that long-continued exposure to sunlight or ultra-violet light may incite cancer, but animals with dark hair do not develop cancer from exposure.' This patient was an albino.

The case

Mr. V. L., aged 62 years, came to the hospital on 6th June, 1943, with a complaint of (1) two raw bleeding swellings, one in the left fronto-temporal region and one in the deltoid region of the left arm, and (2) two ulcers, one on the left side of the nose and one involving the right ear.

History.—About eight years ago the patient noticed two swellings, one on the left arm and one in the left occipital region. Both the swellings were removed by operation. The wounds however took a long time to heal. Since then for nearly six years he had had no trouble of any kind when about 2½ years ago he developed an ulcer on the lobule of the right ear. The ulcer persisted for a long time until the medial half of the lobule was eroded. The ulcer then healed in that region, leaving a clean postero-lateral half of the lobule. But the ulcer then appeared in front of the tragus of the same, i.e. the right ear, and on the inner aspect of the auricle. About 18 months ago he noticed the two above-mentioned swellings—those on the fronto-temporal region and on the arm. He cannot say exactly when the ulcer on the left side of the nose first appeared.

The patient and one of the two brothers are albinos, while the third brother and one sister have normal complexions. No other member of the family is an albino. The patient had taken several intravenous injections about 20 years ago. He does not know the name of the injections and would not tell the reason why he took those injections.

Findings.—W.R. and Kahn tests are negative. The urine does not show any abnormal constituents.

1. Arm swelling: A cauliflower-like fungating slightly flattened swelling about 3 inches in diameter is situated in the region of the deltoid muscle on the lateral aspect of the left arm. The tumour has a pedicle about 2 inches in diameter, and it appears as if this pedicle is growing out of an opening in the skin. The growth has a hard edge, and the whole growth is nodular on the surface. It is not attached to the deeper tissues, for on contracting the deltoid muscle the tumour can be moved about quite freely. The tumour is situated just below the scar of the previous operations. In this operation scar about 1 inch below the tip of the acromion can be felt a small hard nodular mass about ¾ inch × ½ inch. This mass is completely covered with the scar to which it is adherent. On contracting the deltoid muscle, the mass becomes slightly anchored.

2. The fronto-temporal tumour. This tumour is raw and fleshy-looking, but almost smooth on the surface, and bleeds easily on touching. It is about

2½ inches × 2 inches × 1½ inches, and feels fixed to the subcutaneous tissues (figure 1, plate XXI).

3. A small triangular superficially ulcerated area is situated on the left side of the nose. The ulcer has an irregular rolled thickened edge (figure 1a, plate XXI).

4. There is a superficially ulcerated area about ½ inch in diameter in front of the tragus of the right ear. The inner surface of the auricle is also ulcerated in places, and, as already mentioned, one half of the lobule has been lost. The remaining half is clean. The ulcer has no definite palpable edge, and it is painful on touching. This is the only ulcer which is painful (figure 2, plate XXI).

5. In the left occipital region there is a well-formed scar.

Treatment and further progress

1. The tumour on the left arm was excised and sent for microscopical examination. The report was: 'the tissue shows solid finger-like or branching processes of epithelial tumour tissue extending into the deeper layers of the skin. The processes are made up of a peripheral single layer of cubical cells and a central mass of loosely arranged polymorphous cells. The nuclei of these cells are ovoid and regular and relatively poor in chromatin. There are a fair number of cells undergoing mitosis, but there is no marked atypia. There are areas which show an adenoid structure with a central space. Diagnosis: Adeno-cystic epithelioma'.

After excision, in view of the report of malignancy, it was not surprising to find that the operation area instead of healing became covered with coarse rapidly growing granulations, resembling the original tumour. This fresh vigorous growth was now treated with surface application of radium needles—the total dosage given being 1,101.0 mg. hours. The growth then completely and rapidly retrogressed, the raw area became covered with epithelium and within a few weeks there was a supple, thin, bluish-papery scar with fine blood vessels which could be seen just under the surface.

2. The tumour on the fronto-temporal region was treated with interstitial radiation, the total dosage given being 1,593.6 mg. hours. The biopsy report of this tumour is the same as for the growth on the arm—adeno-cystic epithelioma. The tumour completely disappeared and was replaced by a thin papery scar.

3. The ulcer on the left side of the nose clinically appeared like a rodent ulcer, but the biopsy report was as for the other two growths, adeno-cystic epithelioma. This ulcer growth was treated by surface application of radium and is completely healed with a dosage of 109.2 mg. hours.

All the above three ulcer growths remained completely healed till the patient's death (about January 1945). With the available apparatus, the inside of the right ear which was ulcerated could not be adequately treated, and the patient refused to take treatment at any other institution.

The patient returned in October 1943, complaining of a swelling in the left pre-auricular region. The swelling was fluctuating and slightly painful (figure 3, plate XXI). This swelling was treated by exposures to a deep x-rays and by January 1944 the growth had completely disappeared (figure 4, plate XXI).

In September 1944 the patient again returned complaining of:—

1. Pain in the right side of the chest.
2. An irritating dry cough.
3. A serosanguineous discharging ulcer in the nodular area of the operation done 8 years ago. When the patient had first come in, June 1943, he had refused to take any treatment for this nodular growth.

Findings in September 1944

1. There is a thin papery-bluish adherent scar at the site of the old fronto-temporal region.

2. The ulcer area on the left side of the nose now looks almost like normal skin.

3. The ulcer area on the left arm which was treated with radium is now covered with a thin bluish-papery supple scar under which several capillary vessels can be seen.

4. Just above this healed area there is a necrotic ulcer discharging foul-smelling sanguineous material.

5. There is a deep necrotic painful ulcer in front of the tragus of the right ear. The ulcer on the inner aspect of the right auricle is the same as before, and this ulcerated area is also painful.

6. There is a newly forming small ulcerating growth on the left cheek.

7. A small new growth is appearing on the back of the right arm.

8. A radiogram of the thorax shows an opacity at the base of the right lung possibly adherent to the diaphragm.

10. On examination of the larynx is seen a small, irregular, friable, easily bleeding growth at the base of the epiglottis on the left side. Biopsy of this growth: 'groups and columns of small atypical polygonal cells. The cells have a basophilic cytoplasm. The cell bodies are ill defined. The nuclei are round and ovoid. One to two small basophilic nucleoli. Presence of a fair number of atypical mitoses. The cell columns are separated by a loose connective tissue stroma containing a fair number of thin-walled blood capillaries. A few large polygonal cells with large giant nuclei seen. Presence of a few squamous pearls. Diagnosis: Epidermoid carcinoma, grade 2 intermediate type'.

The ulcerating nodule on the left arm was excised. During the operation it was found that the nodule had sent processes in between the muscle fibres of the deltoid. The wound healed completely within a few weeks. Biopsy report of this nodular growth: Adeno-cystic carcinoma.

The patient refused to have any treatment for any of the other new developing growths and expressed his wish to go to his native village and die in peace.

The patient gradually began to lose in health and died about January 1945.

Special features of the case are—the long history of the disease; the slow progress of the malignant growths; the multiplicity of the primary tumours; the new growths appearing in a crop; the ulceration of the previous operation scar, after a dormant period of 8 to 9 years; a favourable response of the growths to radiation. Clear points were the identical histological appearance of the growths—except the laryngeal growth; more marked affection of the left side of the body—particularly the face and the arm; the albino condition of the skin; the absence of any report of any pre-cancerous condition.

Acknowledgment

I am very thankful to the artist for the photographs and the pathologists for their detailed histological report—Drs. V. V. Gharpure of Tata Memorial Hospital and J. G. Parekh of Sir J. J. Hospital.

Description of the photographs (Plate XXI)

1. Figures 1 and 1a. The fronto-temporal tumour and the ulcer on the left side of the nose.

2. Figure 2, the remaining half of the lobule of the right ear and a newly developing tumour on the left cheek.

3. Figure 3, the swelling which appeared in the left pre-auricular region before deep x-ray therapy.

4. Figure 4, the patient when all the growths had healed after radium therapy and deep x-ray exposures.

A BALLOON CYST OF THE LUNG

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Case report

AHMED, male, aged 19 years, clerk by profession, felt suddenly giddy and extremely weak while working in his office. When going back to his quarters he got out of breath. He began to experience a feeling of gradual bulging of the right side of the chest. With rest in the bed, his dyspnoea partly subsided. He, however, began to have a dull aching pain over the right chest, dry cough, and palpitation.

On examination, there was no cyanosis or clubbing of the fingers. The respiratory rate was 28 per minute; pulse 82, of good volume and tension. The apex beat was displaced to the left by $1\frac{1}{2}$ inches; the trachea also was displaced to the left. There was diminished movement of the right side of the chest. The intercostal spaces on the right appeared to be widened compared with those on the left. There was hyper-resonance and marked diminution of breath sounds on the right side. The 'coin' sound could not be elicited. A radiograph showed a huge balloon cyst occupying practically three-fourths of the right lung (see figure on plate XXI). In order to relieve his dyspnoea and pain, one thousand c.cm. of air were aspirated from the cyst. Immediately after this removal, the displacement of the apex was reduced to quarter of an inch. The intracystic pressure came down from plus 16, plus 20, to -2, plus 3 c.cm. of water. Two days later his dyspnoea and pain recurred. Aspiration of air was therefore repeated. Bronchoscopy revealed that the opening of the right bronchus was slit-like, and was pushed forward. The eparterial bronchial opening could not be seen owing to the presence of some oedema. Ten c.cm. of lipiodol was put into the right bronchus. Subsequent x-ray picture showed lipiodol held up in a markedly dilated lower lobe bronchus, producing a sausage-shaped opacity to the right of the vertebral column. Evidently the right middle and lower lobes were completely collapsed due to the distension of the balloon cyst which was found in the upper lobe. Intrapulmonary injection of lipiodol showed that the whole of the lobe had undergone cystic change. Aspiration was performed eight times at intervals of two days. As he refused surgical interference, he was invalided out of the service. At the time of discharge he was able to move about without much discomfort though mediastinal displacement was still present. A letter from him six months after discharge showed that his condition was stationary.

Discussion.—It is unusual for a balloon cyst of the lung to exhibit symptoms for the first time during adolescence. The patient had no symptoms whatsoever to suggest any respiratory disease until the onset of the present condition. He had even completed two years' active service in the army.

A balloon cyst usually produces symptoms either soon after birth or in the later period of infancy. The patient presents extreme cardiac and respiratory embarrassment owing to increasing distension of the cyst and consequent mediastinal displacement. The case reported by Crosswell and King (1933) and the one reported previously by the writer (1942) were in children. Evidently in this case, silent multiple cysts had been present in the right upper lobe from birth. For some reason the opening of one

of the cysts must have become valve-like, allowing air to get in during inspiration and preventing air getting out during expiration. This must have resulted in ballooning of the cyst, and consequent respiratory embarrassment. I had in mind two methods of treatment neither of which for want of facilities could be adopted. Moreover the patient was unwilling for operation. Collapse of the upper lobe could have been effected by artificial blocking of the eparterial bronchus, a method which was adopted by Brook to collapse tuberculous cavities. Though I succeeded in inducing artificial pneumothorax, the lung could not be completely collapsed because of the very high positive intrapleural pressure produced. The other method of treatment would have been lobectomy.

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TRAUMATIC RUPTURE OF LARGE SPLEENS

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TRAUMATIC rupture of the spleen is one of the most urgent and fatal of abdominal catastrophes. In tropical surgical practice, splenectomy is a fairly common emergency operation which unfortunately carries a high mortality, because the hæmorrhage is usually terrific since the spleen is so commonly grossly enlarged from disease, because lack of adequate ambulance facilities results in delay in transporting those cases which survive to surgical aid. These patients therefore often arrive in very poor condition, and many are moribund or actually dead by the time they reach hospital. They may have to be carried long distances over bad roads in uncomfortable and unsuitable vehicles. Surgical treatment must be prompt and daring, as splenectomy usually offers the only hope of survival.

Pathology

In Asia, by far the commonest cause of splenomegaly is malaria. The spleen is at first moderately enlarged and firm, but in later cases it may become hard and often of enormous dimensions. Amongst native races, the less enlightened classes take quinine for almost any kind of fever until the pyrexia subsides and then discontinue it until another attack supervenes. Chronic cases with very large hard spleens are resistant to medical treatment, though some appear to show some response to the administration of quinine or cinchona mixtures combined with deep x-ray therapy. Malarial therapy combined with splenectomy

offers a fair prospect of permanent cure, but most surgeons who have attacked the problem from this aspect have found the mortality sufficiently high to extinguish their enthusiasm. When improved anæsthetic and transfusion facilities become more readily available, deliberate operative treatment may eventually become more popular. According to surgical textbooks, spontaneous rupture of the diseased or even the normal spleen can occur. It is also well known that the enlarged spleen can be ruptured, resulting in fatal hæmorrhage, by trivial violence. In actual practice, however, despite the comparative vulnerability of the enlarged friable organ, as a rule, rupture appears to be caused by considerable violence, and most of the cases met with are due to traffic accidents, and quite often there are associated injuries. Occasionally cases are seen where the rupture has followed a brawl, especially those in which sticks have been used, or where the victim has accidentally fallen upon or bumped against some unyielding object. In the great majority of cases of rupture of the enlarged malarial spleen, the ensuing rapidly developing shock and hæmorrhage are so severe that the patient succumbs very quickly, and probably not more than one case in twenty ever reaches hospital alive. Of those which are actually operated upon, it is often astonishing to find how severely the organ has been damaged without the bleeding having been fatal within minutes. It is not often appreciated that the spleen has considerable powers of spontaneously arresting hæmorrhage especially after the surrounding pressure has been raised when blood has distended the peritoneal cavity.

An example is shown in the illustration (figure 1, plate XXI) of a spleen which was removed post mortem from an Arab boy of fifteen who was injured in a road accident and sustained fracture of the skull with cerebral injuries, a crushed right chest, and ruptures of the spleen and left kidney. Death occurred on the fourth day from cerebral compression. The large rents in the spleen went right through the substance, but were firmly held together with blood clot, though they could fairly easily be separated.

The amount of blood in the peritoneal cavity was not great, and no doubt there had originally been much more, but some had been absorbed. It is probable that the giving way of such a clot is the common mechanism of delayed hæmorrhage from the spleen following injury. It is stated that delayed hæmorrhage may be due to the bursting of a subcapsular hæmatoma followed by fresh bleeding. It is very doubtful if this phenomenon does in fact occur. If it does it must be very rare, since we have not seen specimens showing any evidence which would lend support to this theory. Neither does omental plugging referred to by Gillis (1944) appear to have much influence in stopping bleeding.

Kala-azar is far less common and confined to certain provinces, especially Bengal and Assam. It may produce very large spleens which are at first soft and extremely fragile, but later they may become firm and fibrous. These spleens can be ruptured by trauma. The tear of the spleen capsule sometimes seen when spleen puncture is cleaned out for diagnostic purpose by a careless or inexperienced worker might also be mentioned here.

Other causes of splenic enlargement such as typhoid fever, tumours, or blood disorders are not important ætiological factors in contributing to the incidence of traumatic rupture. In fact, they have the opposite effect by confining the patient to bed, or at least restricting activity.

When bleeding into the peritoneal cavity from the spleen occurs, the movement of the abdominal viscera causes much of it to become defibrinated. Clots form around the spleen and fix it to the diaphragm, but most of the blood remains fluid. There are many references in surgical literature to the difficulties and dangers of splenectomy occasioned by adhesions between that viscus and the diaphragm. No doubt this is accounted for by the fact that common indications for splenectomy in temperate countries are acholuric jaundice, purpura, and splenic anæmia—conditions in which adhesions may occur. The malarial spleen however much enlarged is seldom adherent to anything. At least this has been our experience in India, Iraq and Persia.

Diagnosis

The patient generally arrives at hospital in a condition of profound shock with shallow respiration. Local signs of trauma or fractures of the left ribs, possibly with lung complications, may point to a damaged spleen. Hæmaturia is not uncommonly present from coincident injury to the left kidney. There is pain and tenderness in the left hypochondrium, and pain is often referred to the left shoulder. The abdomen becomes distended with blood and gas, because often there is intestinal stasis with a tendency to ballooning of the gut, and respiration is therefore embarrassed. True rigidity of the abdominal wall is usually absent. The pulse is rapid and thin, and the blood pressure is low. X-ray examination may show raising of the left cupola of the diaphragm and diminished respiratory excursion. Radiographic examination should not be attempted, if diagnosis can be made without it, since it distresses the patient who is already in a critical condition, and time is wasted unnecessarily. Ballance's sign, that is to say fixed dullness in the left flank and shifting dullness in the right, is an unreliable diagnostic sign, as it depends on the size of the spleen, the amount and site of blood clot, and the quantity of gas in the bowel. Liver dullness sometimes appears to be diminished, leading to suspicion of injury to the hollow viscera. This is possibly due to



Fig. 1.—X-ray plate showing an opacity in the region of the right upper lobe of the lung.



Fig. 2.—Photograph of the cut surface of the tumour of the lung.

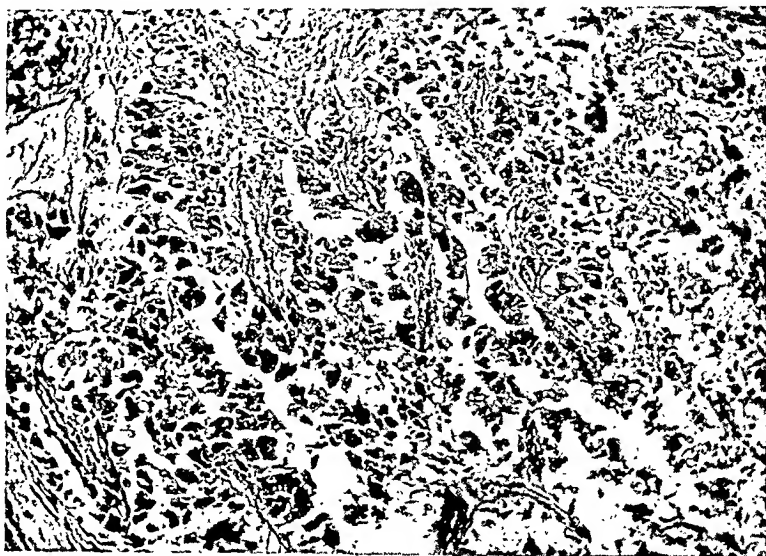


Fig. 3.—A low power photomicrograph showing a structure of an adenocarcinoma.

PENICILLIN IN CANCRUM ORIS COMPLICATING KALA-AZAR : P. C. SEN GUPTA
AND N. K. CHAKRAVARTY. PAGE 542.



Fig. 1.—Case 1. Extensive cancrum involving cheek, lip, root of nose and nasal septum.



Fig. 2.—Case 1. After treatment.



Fig. 1.



Fig. 1a.

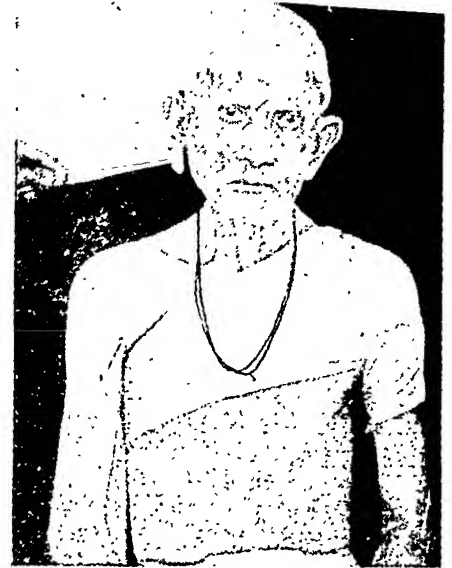


Fig. 2.



Fig. 3.



A BALLOON CYST OF THE LUNG : R. VISWANATHAN. PAGE 547.



Figure shows balloon cyst occupying almost the whole of the right side. The outer and lower border of the cyst is represented by the curved line in the costo-phrenic angle. The upper and inner margin is shown as a thick curved line overlapping the sterno-clavicular junction. Dense opacities are due to the lipiodol in the smaller cysts.

TRAUMATIC RUPTURE OF LARGE SPLEENS : F. V. STONHAM. PAGE 547.

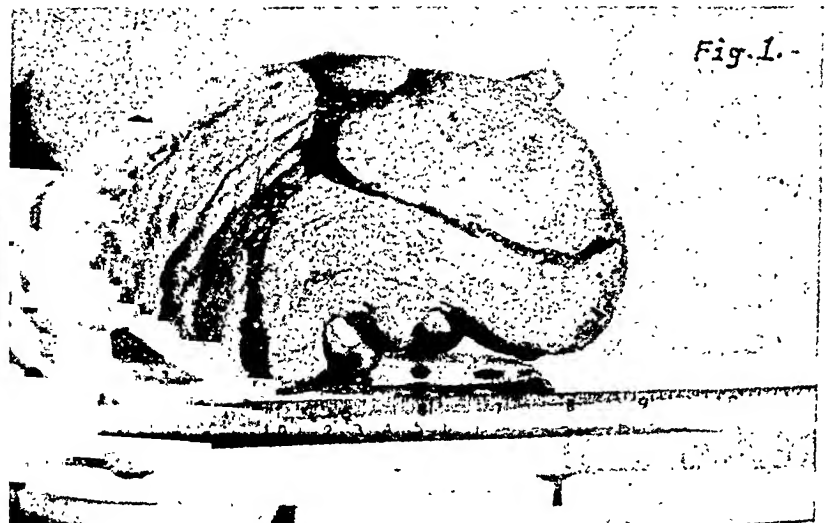


Fig. 1.

Fig. 1.—Spleen showing rents which go completely through the spleen substance yet are firmly held together with clot.

the large quantity of blood permitting coils of bowel to pass up in front of the liver.

The urine should always be examined. We have seen an instance of rupture of the left kidney without damage to spleen, or other viscera in a patient who fell from a cycle and struck his abdomen against a stone.

There is usually little or no recovery from the initial shock. The patient's condition tends to deteriorate progressively and, unfortunately, often rapidly, though in some cases the condition may remain in an apparently stationary condition for many hours even during a journey.

Treatment

Prompt operation is the only treatment which will save life. Time spent in resuscitation may be time well spent with other abdominal emergencies, but if the spleen is ruptured, it is valuable time wasted. No delay is permissible. In instances where we have had full facilities for expert anaesthesia and transfusion, and have attempted to improve the patient's condition before operating, the results have compared unfavourably with pre-war experience in India, where saline was the only fluid available for intravenous infusion, apart from what blood could be removed from the peritoneum; and the anaesthetic used was chloroform. Attempts at a resuscitation cause further bleeding, further shock, and added respiratory embarrassment from increased pressure on the diaphragm.

The only possible exception is the case which is more than twelve hours old when first seen, and the degree of shock is moderate and the patient's condition remains stationary. Under these circumstances it may be assumed that clotting has occurred and that bleeding is for the time being, at any rate, in abeyance. In such instances the approach may be more deliberate, and the optimum time for intervention chosen. This incurs some risk of the effects of anoxia from anaemia, stagnation, and depressed breathing. However in these cases, recovery without operation is not altogether outside the bounds of possibility. Late cases carry a very high operative mortality.

Splenectomy

Anaesthesia

Ether is undesirable since it increases shock and haemorrhage and stimulates respiration which is already mechanically interfered with. Nitrous oxide and oxygen has not these disadvantages but is apt to result in anoxaemia. Cyclopropane is preferable when available, since a high ratio of oxygen can be given with it.

Local infiltration is impracticable since intra-abdominal manipulations against the diaphragm have to be carried out; and the patients are usually too shocked for spinal analgesia. Chloroform carries the theoretical objection of

alleged toxicity, but in practice it is excellent. It does not produce any increase in respiratory excursion, nor does it tend to cause increased haemorrhage. It has the added advantage of giving good relaxation. Any objection to chloroform is academic rather than practical, and most of the writer's successful cases before the war were done under chloroform anaesthesia given with Junker's apparatus and a simple vulcanite mask which does not accurately fit the face, thus ensuring that there is always plenty of air. Oxygen should be given as well. A cylinder can be connected to the Junker's apparatus instead of the bellows.

Continuous pentothal has been used in some more recent cases, and it appears to be quite satisfactory. As the operation is started, an intravenous saline apparatus should be arranged and blood should be ready. The rate of intravenous fluid should be controlled by the anaesthetist, since severe shock is inevitable at two stages of the operation, first when the abdomen is opened and pressure on the abdominal contents is released, and second when the spleen is dislodged from its bed.

There is no objection to commencing the intravenous infusion with a pint of saline, since it overcomes any possible viscosity of the circulating blood, and the unclotted blood recovered from the abdomen may be poured into it through a gauze strainer without citration. Citrated blood from a bank or donor is nearly always required in addition.

Incision

Splenectomy for haemorrhage is one instance in which the surgeon is justified in working against the clock, and the incision should therefore be the one which is most readily made and closed, and must be of ample proportions. A long mid-line incision is by far the best (figure 2). A transverse muscle cutting incision may be added if further room is needed, but this is seldom required for enlarged spleens, since the larger the spleen the nearer is the pedicle to the mid-line.

An alternative incision for very large spleens is a seven-inch mid-line incision which starts below the umbilicus and ends at the supra-umbilical tendinous inscription of the rectus abdominis, which is incised laterally converting the incision into an inverted 'L' (figure 3). In most subjects the rectus at this level is wide enough to permit the lateral incision to end at the costal margin. It is not necessary to suture the rectus to the sheath, since it does not retract if the incision cuts accurately or slightly obliquely through the tendinous inscription. This incision gives ample room and is fairly easy to close, and has the advantage that no nerves are cut. Other approaches such as left Kocher's, Perthes', Morison's, or paramedian are not recommended for emergency operations in tropical countries where the spleen may be very large.

Operation

The incision should be completed through all tissues down to the peritoneum, which appears blue from the underlying blood. If the peritoneum is widely incised at this stage, not only

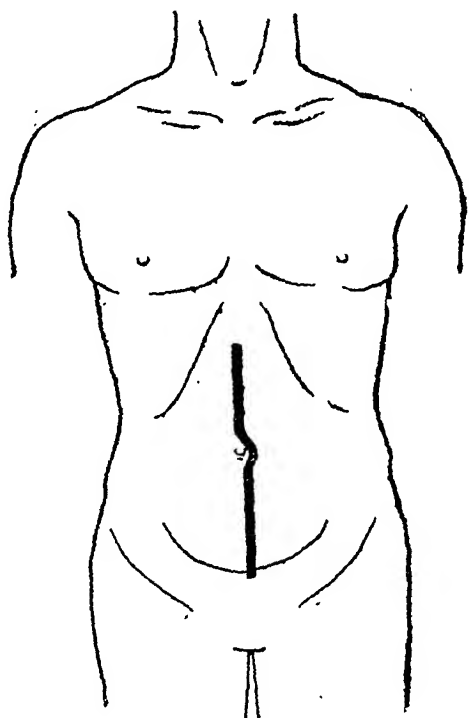


Fig. 2.—Incision for splenectomy.

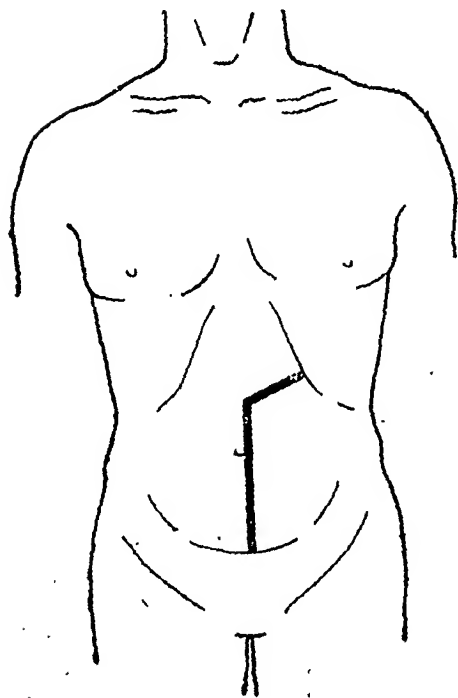


Fig. 3.—Alternative incision for very large spleens.

will there be sudden relief on tension cause a sharp fall in blood pressure, but much of the blood will be lost. A small opening can be plugged with the finger pending the insertion of a rubber tube; or a Higginson syringe so that

the blood can be collected in a suitable vessel and restored to the circulation by pouring it into the saline infusion apparatus. The peritoneum is then opened widely, and any blood remaining bled out and separated from clots and utilized in a similar way. After a rapid survey of the abdominal contents, the hand is passed between the spleen and the parietes to which it is usually glued by clot, and gently separated.

Any firm adhesions if present are divided between clamps or by diathermy. As pointed out by Henry (1940), the upper pole should be delivered first as this is usually easier. This is done by passing the hand over the diaphragmatic surface and turning the organ downwards and to the right and pushing the left edge of the incision underneath it, and thus delivering it out of the wound. The spleen has two pedicles. That is to say it lies at the apex of a pocket-shaped process of the peritoneum. The gastro-splenic ligament which forms anterior half of the pocket contains the short gastric vessels, and the lienorenal ligament, or posterior half of the pocket, contains the splenic vessels. Often the two structures are so suffused with blood and covered with clots that only one large pedicle is recognizable, and nothing is gained by attempts to separate them. The pedicle is divided in sections between forceps, keeping as close in to the spleen as possible to avoid injury to the tail of the pancreas and the fundus of the stomach. Gall-bladder forceps are useful for this purpose. After the pedicle has been divided between forceps and the spleen removed, each leash of vessels is ligatured and the remaining forceps are removed. As an additional safeguard, all the larger vessels can be tied separately and after the spleen has been removed, as the pedicle can more easily be examined, and a mass ligature can be tied around the entire pedicle, as an even further safeguard. A sudden fall off in the patient's condition is often observed when the spleen is dislodged from its bed, and a towel should be packed in temporarily as it is removed. There might be possibilities in the use of a rubber balloon to occupy this space to prevent shock, a manoeuvre recommended by Henry with the object of preventing post-operative lung complications.

The wound is closed as rapidly as possible, and since the abdominal wall is usually slack following previous distension, this is easy whatever anæsthetic is used. Drainage is only employed when it is suspected that the tail of the pancreas might have been injured.

After-treatment

The patient is returned to bed and kept flat or with the shoulders slightly raised and the foot of the bed on blocks to relax the abdominal incision. Transfusion is continued until the systolic blood pressure is in the vicinity of 100 mm. of mercury, after which it should be continued for several hours as a slow drip.

The complication to be most feared is failure to recover from the shock. This may be due to previous anoxia. In such an event, transfusion causes only transient increase in systolic blood pressure, without much improvement of the diastolic pressure, and the pulse rate remains high. Apart from a left pleural effusion which is as a rule moderate in amount and of little significance, other post-operative complications are not frequent. The wound should be carefully watched to forestall dehiscence especially if there has been any doubt about the integrity of the pancreas. The pancreas may be damaged during operation, but traumatic ruptures of the pancreas are very rare (Curr, 1945).

When splenic rupture is complicated by injuries of other viscera, these must receive appropriate treatment at the same time, but the prognosis is of course much less favourable. Simultaneous rupture of the kidney, probably the commonest complication, can in most cases be treated on conservative lines, though sometimes the kidney can be dealt with through the same incision. Associated injuries of the chest are more likely to cause trouble during convalescence.

Conclusion

Rupture of the grossly enlarged spleen is one of the most critical of surgical catastrophies. The hæmorrhage is generally so appalling that death occurs in a few minutes or in fact almost instantaneously. Only a few of these cases reach the surgeon, whose slogan should be *nil desperandum*. Unless the patient is almost completely moribund on arrival, operation offers the only chance of survival and should be undertaken without delay. The surgeon must therefore be daring, and a high operative mortality has to be accepted if lives are to be saved at all. Delay in operating is only justifiable when the patient's condition is so low that immediate operation would be obviously futile, and, contrarily, in those cases where the patient has been injured many hours previously, and the condition has remained good and is not deteriorating.

Summary

1. The pathology and management of cases of rupture of large spleens have been discussed.
2. The tendency for spontaneous arrest of hæmorrhage has been emphasized.
3. The diagnosis of ruptured spleen is considered.
4. Operative details of splenectomy for rupture have been given.

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THE COMPLEMENT-FIXATION REACTION IN GONORRHŒA

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THE complement-fixation reaction in gonorrhœa has not been applied widely like the Wassermann reaction in syphilis. There are three reasons for this: (1) A good antigen has been believed to be not easy to prepare. Specially selected strains of the bacterium have been considered necessary, and special preparations, 'toxins' and lysates have been preferred to the simple bacterial suspensions (Kolmer, 1923, 1929; Osmond and Oliver, 1929). (2) The reaction is not a strong one. (3) The reaction is not so constantly positive in gonorrhœa as the Wassermann reaction in syphilis.

The writers have taken advantage of the antivenereal disease drive in Calcutta, and have studied the reactions of unselected samples of blood received from clinics for the Wassermann reaction. They find that, in spite of its limitations, the reaction has its utility. Their technique, observations on the technique, and reactions of sera from 100 unselected cases of venereal disease are presented in this communication.

The technique

The hæmolytic system.—This is taken from the Wassermann reaction as performed in this laboratory (Greval, 1943), the essential features of the technique being (i) standardization of the red blood corpuscle (rbc hereafter) suspension colorimetrically (Greval, 1929; Greval, Yesudian and Choudhury, 1930) and (ii) classification of the complement (Greval, Chandra and Das, 1940).

The classification of the complement being a new item is summarized.

It is based on the titration of the complement in the presence of the Wassermann reaction antigen in accordance with Method No. 4 of the (British) Medical Research Council (1918, then Committee). Ideally and typically, the front row of tubes (without the antigen) should indicate the MHD in a 1 in 40, 1 in 50 or 1 in 60 dilution. This is the optimal titre. A titre below 1 in 40 is low. A titre above 1 in 60 is high. Again ideally and typically, the back row of tubes (with the antigen) with twice the quantity of the complement should indicate the MHD. The complement then is of optimal reaction. If the quantity needed is less than twice, the complement is 'cholesterol-fast'. If the quantity needed is more than twice, the complement is 'cholesterol-shy'.

For the reaction in gonorrhœa, the complement is preferred in the following order: (1) one of optimal titre and reaction, (2) one of high titre and optimal reaction, (3) one of high titre alone, and (4) one of optimal titre alone. Complement of other qualities is not used.

The antigen.—A gonococcus vaccine is used containing 500 million organisms per c.c. The writers obtain their supplies, in 1 c.c. ampoules, from the Central Research Institute, Kasauli, and find them satisfactory. The polyvalent character of the vaccines and the time taken in ampouling it have been described thus :—

'The seed of our gonococcus vaccine is selected to include six strains, if these are available at the time of preparation, but at least two strains are used for each brew.

The interval between washing and ampouling may vary, depending on supply and demand, from about one month to six months' (Mulligan, 1945, personal communication).

The need for polyvalency in gonococcus suspensions for the purpose of this reaction has

that, any time before the heavy meal of the day will do.

Known positive serum.—A positive serum of known titre is diluted 1 in 5 with saline containing 0.25 per cent trikresol and kept in the refrigerator.

Known negative serum.—When a positive serum is available, only 1 negative serum is enough as a control. Otherwise at least 6 controls, 3 from positive cases of syphilis and 3 found negative in the Wassermann reaction, are required. Serum from a subject with a bad throat (likely to harbour gram-negative cocci of the genus *Neisseria*) may also be included.

Charging of tubes.—Four tubes are required for each case and charged thus :—

T u b e s				
For serum control		For test proper		
1st	2nd	3rd	4th	
1 vol. of serum dilution 1 in 5	5	5	10	20
Antigen	1 vol.	1 vol.	1 vol.	1 vol.
1 vol. of complement dilution containing	1½ MHD	1½ MHD	1½ MHD	1½ MHD
<i>Antigen and complement are mixed and delivered as a double volume.</i>				
Saline	1 vol.	1 vol.	1 vol.	1 vol.
Later (<i>vide infra</i>) sensitized rbc	1 vol.	1 vol.	1 vol.	1 vol.

been overstressed. Even if evidence of several strains be admitted, there remains one very large main group (Tulloch, quoted by Topley, 1933) which is representative of the species. The strains are not comparable to the types of meningococcus.

A 1 in 5 dilution of the contents of one ampoule from each batch of the vaccine is tested for hæmolytic and anticomplementary activity, thus :—

(1) Tube 1. Three vols. of vaccine 1 in 5 are incubated with 1 vol. of sensitized rbc suspension for ½ hour. There should be no hæmolysis. An excess of the antigen is taken to exclude a possible action on prolonged contact.

(2) Tube 2. One vol. of vaccine 1 in 5 is incubated with 1 vol. of complement dilution containing 1 MHD and 1 vol. of saline. One vol. of sensitized rbc is then added and the tube reincubated for ½ hour. The hæmolysis should be complete. The tube will be slightly hazy due to the vaccine and the debris of lysed rbc. A ruby-red and crystal-clear tube is not aimed at.

The test

The serum under test.—It is inactivated immediately before use and diluted 1 in 5, 1 in 10, and 1 in 20. If possible, it should be taken in the laboratory from the patient: otherwise it should be taken and preserved with special care and not allowed to become anticomplementary. The ideal time for taking blood is the early morning before food is taken. After

The tubes without the addition of rbc are left: (i) At room temperature for ½ hour, (ii) in incubator for ½ hour, (iii) at room temperature for 5 to 10 minutes, until the tubes do not feel warm, (iv) in an ice box for ½ hour, (v) at room temperature for 5 to 10 minutes, until moisture does not condense on the tubes.

The order is important. If the tubes are left in the ice box first, the anticomplementary action of some old sera becomes more marked.

Finally 1 vol. of sensitized rbc is added to each tube and the tubes are incubated for half an hour.

An antigen control is included for the day's work. It consists of (i) antigen 1 vol. +, (ii) complement 1 MHD +, (iii) saline 1 vol. It is left at the various temperatures in the same rack as the other tubes and tested for loss of complement by adding rbc suspensions 1 vol. The rbc should be almost completely hæmolyzed.

Reading of results.—The results are read (i) immediately for ± and −, and (ii) next day for + and T (trace of hæmolysis), after the tubes have stood in the ice box overnight. A ? — reading is ignored and classed with −.

The positive and negative controls (at least the majority of negative controls) should give the expected reactions.

Record and report

1. When the serum control is fully hæmolyzed. A + reading recorded under its appropriate

tube is reported as 'positive in 1 in 20', 'positive in 1 in 10' or 'positive in 1 in 5'. A reading of T or \pm in one or more tubes is recorded under each tube and reported 'doubtful'. A sustained partial but well-marked inhibition of hæmolysis in all tubes is more important than a \pm reading in one tube (the 2nd tube with serum 1 in 5) only. The history will decide the significance in all cases read as \pm .

2. When the serum control is partially hæmolysed (\pm). A + reading in the 3rd and 4th tube is reported as 'positive in 1 in 10' or 'positive in 1 in 20'. For a + reading in the 2nd tube only, the serum must be diluted and tested until the 1st tube is fully hæmolysed.

3. When the serum control is not hæmolysed at all or shows only a trace of hæmolysis (reading + or T). Record + or T. No report is possible. Dilute the serum for further tests.

Observations on the technique

The quality of complement fixation.—The reaction, though specific, is weak. Because of this weakness, some workers do not employ a fixed period of incubation after adding the rbc suspension. The incubation is continued, while the tubes are being examined again and again, until the expected reaction is obtained. The inhibition of hæmolysis under such conditions is not perfect, and the reaction is hardly repeatable.

It may be added that the positive rate increases with the duration of the infection, and especially with the onset of complications of the sub-acute and chronic stages. The reaction, therefore, is likely to give aid when such an aid is most needed. Unlike the Wassermann reaction, however, it is not positive in all cases of gonorrhœa even in the chronic stages.

For acute and sub-acute cases there is hardly a need for the reaction.

The European figures given by Topley (*loc. cit.*) are as follows:

Type of infection	Cases positive, per cent
Acute gonorrhœa	48
Sub-acute and chronic gonorrhœa	61
Epididymitis	82
Prostatitis	80
Vesiculitis	88
Metritis	68
Salpingitis	77
Vulvo-vaginitis	50
Arthritis	82

It may also be added that the weakness of the reaction is a feature of this class of complement fixation (between bacterial and antibacterial sera). Stronger reactions cannot be expected.

Special features of the technique.—There are six such features: (1) the antigen is easily available, (2) the dose of the antigen is linked to

the MHD of the complement, (3) the dose of the complement is restricted as much as possible, (4) complement of a poor quality is not used, (5) cold fixation is also employed, and (6) a perfect inhibition of hæmolysis is insisted upon for a + reading although T and \pm readings are considered significant.

Repetition of the reaction

1. *For technical reasons.*—From what has been said concerning the preference for the qualities of the complement, it follows that a doubtful reaction, not in accordance with clinical expectations, or not giving enough aid in diagnosis, should be repeated with a complement of a better quality (if an inferior quality has been used before) in order to obtain more fixation. This is necessary in view of the fact that certain adjustments possible in the Wassermann reaction cannot be made in this reaction.

The repetition is also indicated when the MHD of the same lot of complement has given a fixation rather on the low side in the Wassermann reaction.

Enough serum should be available for the repetition from the original sample. If a fresh sample is necessary, the preparatory measures must now be enforced if they have been ignored previously: (i) Taking the blood early in the morning before any food has been taken, and (ii) ensuring the sterility of the serum which should if possible not be anticomplementary at all.

2. *For observing the course of the disease.*—Fresh samples may be taken from time to time for observing increasing or decreasing fixations.

3. *For test of cure.*—The repetition will be of limited value: (1) If a positive or significantly doubtful reaction has never developed during the course of the disease, a negative reaction later is no proof of freedom from gonorrhœa. (2) A positive reaction is against a cure, although there are 'many cases which clinically and bacteriologically are to be considered as cured, and which even subsequent history likewise fails to incriminate, which have provided very slow falling off in the strength of the reaction over a period of many months and up to one year' (Osmond and Oliver, *loc. cit.*). (3) A positive reaction turning negative is in favour of a cure.

Summary

1. A complement-fixation test for gonorrhœa can be performed with a simple gonococcus vaccine used as antigen. The hæmolytic system is taken from the Wassermann reaction. The complement is selected with respect to quality, and is restricted in quantity. Cold fixation is added. Grades less than a fully positive reaction (complete inhibition of hæmolysis) are significant.

2. In spite of the weakness of this type of reaction (between bacterial and antibacterial

Results of complement-fixation test in 100 unselected venereal disease cases

Number	COMBINATIONS				Cases in each combination	Result	Report
	Tubes						
	1	2	3	4			
I	—	—	—	—	40	—	Negative.
II	—	±	—	—	3	±	Doubtful.
III	—	±	±	±/—	31	±	Doubtful.
IV	—	T	±	±	4	±	Doubtful.
V	—	+	T/±	T/±	4	+	Positive.
VI	—	+	+	+/T	2	+	Positive.
VII	—	+	±	—	1	+	Positive.
VIII	±	T	T	T/±	1	±	Doubtful.
IX	± (<)	± (≈)	±	±/—	14	±	Doubtful.
					<hr/> 100		

Seven cases gave clear-cut positive reactions. All were found to be cases of gonorrhœa.

Fifty-three cases gave doubtful reactions, dependent on the history for interpretation. Eighteen were found to be cases of gonorrhœa, 18 were indefinite and 17 could not be traced.

Forty cases gave clear-cut negative reactions. They were not enquired into, as a negative reaction is known to be given in the absence of chronicity or complication.

Nearly all the patients had taken the risk.

The reactions of most of the patients were not repeated with a different complement.

The rate of the positive or doubtful reactions is only the rate of the venereal clinics in Calcutta, not of the general population. The daily average at the clinics in August 1945 was 820 (New 110, Old 710). The total civil population of Calcutta, at present, is of the order of 3 millions.

About 33 per cent of cases suspected to be suffering from syphilis were found to be suffering from gonorrhœa in addition.

sera), and the inconstancy of a positive reaction, in the disease the test can be employed in detecting uncured cases and complications.

3. The rate of the positive and doubtful reactions in the patients from venereal clinics of Calcutta is given.

Acknowledgments

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PNEUMO-PERITONEUM IN THE INVESTIGATION OF THE RIGHT COSTO-HEPATIC AREA

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THE authors wish to draw attention to the great value of pneumo-peritoneum in the x-ray investigation of lesions in the right costo-hepatic area. This area is notorious for its diagnostic problems, especially in countries where amœbic hepatitis is common. The customary radiological proceedings of fluoroscopy and the taking of a film may still leave problems unsolved. The further elucidation of these problems often rests on whether a lesion lies above or below the diaphragm, or whether distortion in a clearly visualized diaphragm contour is caused by a deformity of the liver itself. In such cases the procedure of pneumo-hepatography is useful, for by it the diaphragm may be separated from the clearly outlined subjacent surface of the liver.

The general method of pneumo-peritoneum in x-ray diagnosis has been comprehensively reviewed by Maxfield and McIlwain (1944) who also give references. Our own attention was drawn to its possibilities in the investiga-

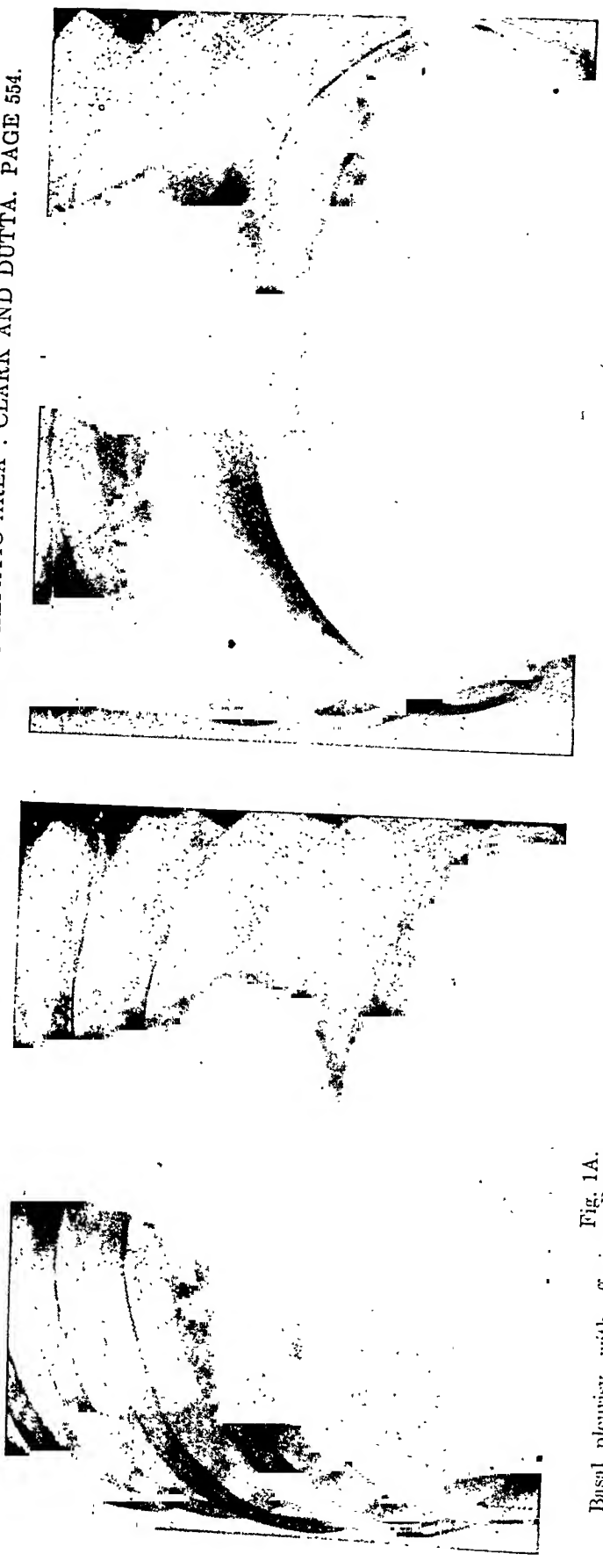


Fig. 1A.
Basal pleurisy, with effusion. Pneumo-hepatography serves to demonstrate the site of the lesion, and the normal liver below the diaphragm (B).



Fig. 1B.

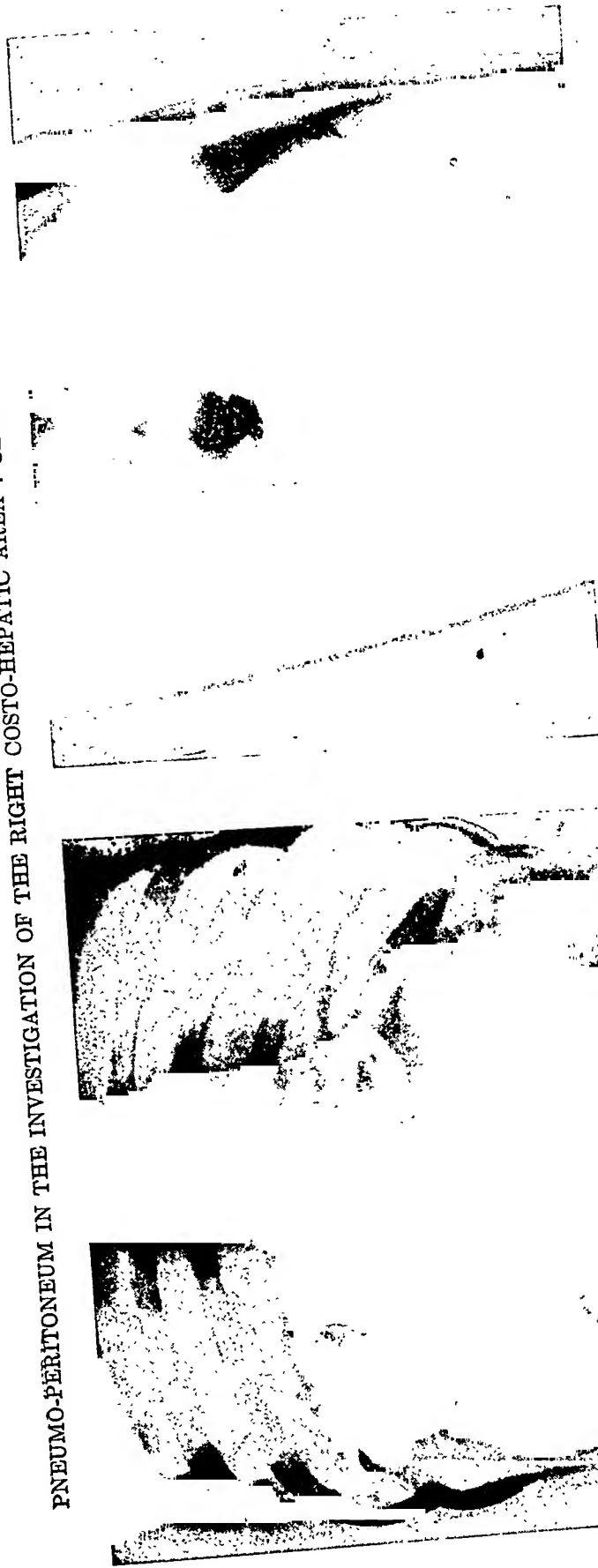


Fig. 3A. The liver, gall-bladder and spleen are well outlined by air, and adhesions to the right diaphragm are demonstrated.

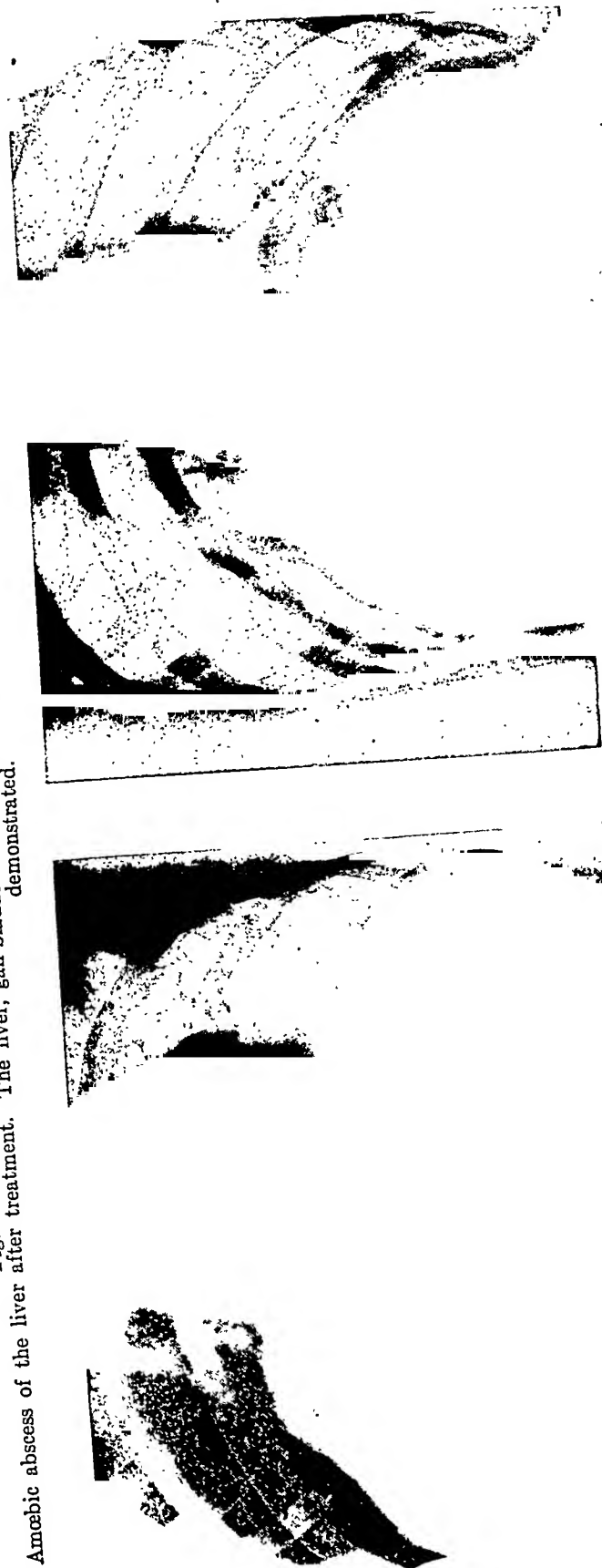


Fig. 4A. Liver distortion probably secondary to acquired deformity of the diaphragm. Before (A) and after (B) introduction of air.

PLATE XXIV

PNEUMO-PERITONEUM IN THE INVESTIGATION OF THE RIGHT COSTO-HEPATIC AREA : CLARK AND DUTTA. PAGE 554.

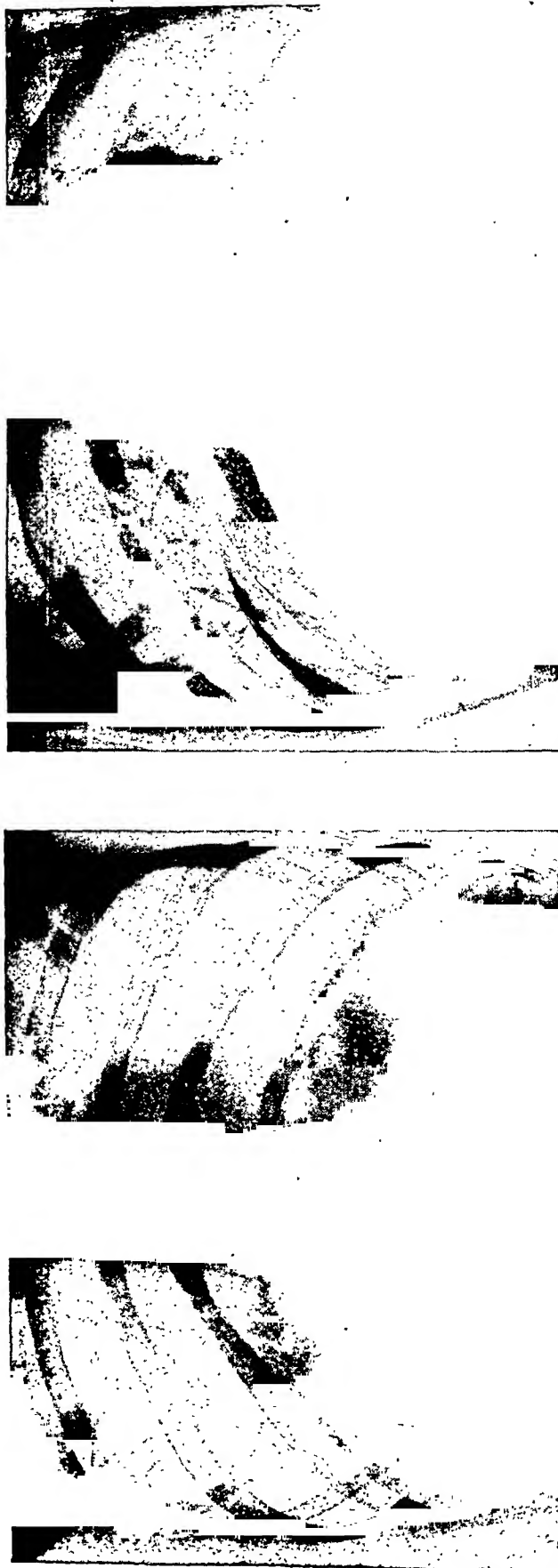


Fig. 5A.

'Hump' deformity suggesting liver abscess (A), shown by pneumo-hepatography to be imposed on the normal liver by a developmental deformity of the diaphragm (B).

Fig. 5B.

PLATE XXV
PNEUMOPERICITONEUM IN THE INVESTIGATION OF THE RIGHT COSTO-HEPATIC AREA : CLARK AND DUTTA.



Fig. 6A.

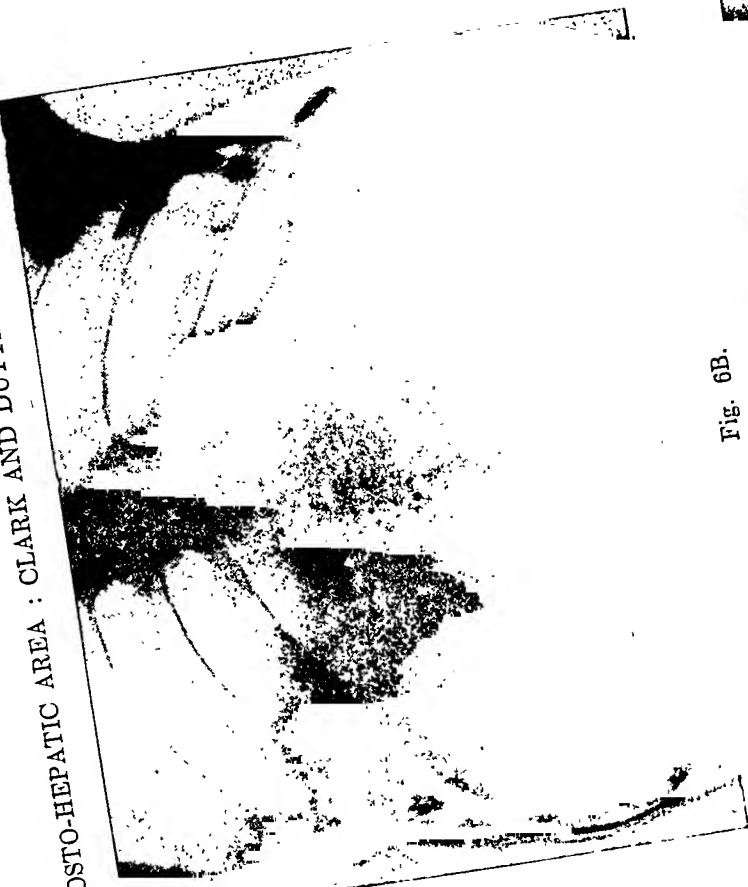


Fig. 6B.



Fig. 6C. The lobulation of the upper surface is brought out after introduction of air (C and D).



Fig. 6D.

tion of the upper hepatic surface while fluoroscoping patients with pneumo-peritoneum induced for pulmonary tuberculosis as described by Dongrey (1941). Clark, Bercovitz and Jones report briefly on its use in the diagnosis of deformities of the contour of the dome of the liver. The present note is designed to give wider publicity to what we consider a very valuable diagnostic help in this area of the body.

The procedure has been used on 35 occasions in the hospital of the Assam Oil Company up to the present time. No ill effects have been observed save for occasional slight transient shoulder pain and, in one case, more severe pain and dyspnoea which lasted about six hours. In this case, 400 c.cm. of air had been introduced in an elderly patient with a rigid and emphysematous chest; we consider that this contra-indication should be added to the two given by Maxfield and McIlwain (1944), *viz*, cardiac insufficiency and an acute infection.

Recently Aslett and Jarman (1945) reported two fatal reactions following pneumo-peritoneum carried out for pulmonary tuberculosis. In one case, symptoms appeared 56 hours after the 14th refill, and in the other 31 hours after the 4th refill. Commenting, Richards (1945) quotes a fatal case of proven air embolism occurring on the fourth day after pneumo-peritoneum. It would thus appear safer to use carbon dioxide which is rapidly absorbed in the body, in preference to air, performing the x-ray examination immediately injection has been completed. Maxfield and McIlwain use large quantities of this gas (3,000 c.cm. or more) for general survey of the peritoneal cavity.

The technique employed is as follows. Morphine grain $\frac{1}{4}$ is given as premedication. The patient lies on its back with the head of the bed raised on 8 to 12-inch blocks. Air is delivered from a pneumothorax apparatus connected to an 18 or 20-gauge needle. The site of puncture, one inch to the left of and below the umbilicus, or about an inch below in the midline, is infiltrated to the peritoneum with local anaesthetic. After the needle has punctured the skin, the manometric level is adjusted to 20 cm. of water. The needle is then introduced further in a slightly oblique direction. When the manometer shows a sudden fall of about 5 cm. or over, indicating that the peritoneum has been pierced, a free flow of air is permitted. Three hundred and fifty c.cm. to 500 c.cm. have been found sufficient for clear separation of the diaphragm from the liver in Indians of slight to average build. Fluoroscopy in the standing position is performed four to eight hours later. If the air accumulates below the right diaphragm, and a more even distribution under both leaves is desired, the patient is turned on his right side for a few minutes before standing for fluoroscopy. The spleen, as well may often thus be visualized.

The following case notes, given in summary, indicate the value of the procedure as a diagnostic aid:—

Case 1.—Indian male, age 26, admitted with right basal pleurisy and a small effusion. He gave a history of jaundice and hepatic pain ten months previously. Pneumo-hepatography showed a normal liver, tending to exclude the possibility of an active primary liver infection (figure 1, A and B, plate XXII).

Case 2.—Indian male, age 34, admitted with right hepatic and shoulder pain. He was afebrile, but polymorphonuclear leucocytosis was present. Distortion of the right dome of the diaphragm was suggestive of a small liver abscess. This 'hump' was shown to be hepatic in origin by the introduction of air, and its resolution with emetine therapy was observed (figure 2, A and B, plate XXII).

Case 3.—Indian male, age 30, admitted with a large amoebic liver abscess. From this, in all, 3,390 c.cm. of 'amoebic' pus, later contaminated with bacillus pyocyaneus, were aspirated. Pneumo-hepatography was used to visualize the final liver outline, and revealed evidence of adhesions between the right lobe and the diaphragm. The gall-bladder and spleen were also clearly outlined. This case is also reported elsewhere by Clark, Bercovitz and Jones (figure 3, A and B, plate XXIII).

Case 4.—Indian male, age 35, admitted with upper abdominal and right hepatic pain, consistent with amoebic hepatitis. Irregularities in the contour of the diaphragm further suggested abscess formation. Injection of air showed a smooth left lobe and distortion of the diaphragm on the right. Adhesions, very evident on fluoroscopy, tethered the apex of a persistent liver protrusion to the concavity of this distortion. Emetine medication was followed by no change in the liver outline. A liver distortion secondary to abnormality, probably acquired, of the diaphragm was diagnosed. A sub-hepatic abscess had been evacuated four years previously after events suggestive of perforation of a peptic ulcer (figure 4, A and B, plate XXIII).

Case 5.—Indian male, age 24, admitted with icterus and an enlarged and tender liver. Radiography showed a localized rounded deformity of the right dome of the diaphragm suggestive of liver abscess. Introduction of air showed a smooth hepatic contour, and a diaphragmatic abnormality corresponding in outline to the former apparent liver deformity. The course of the disease confirmed the presumptive diagnosis of infective hepatitis (figure 5, A and B, plate XXIV).

This type of 'hump' deformity in the contour of the right dome, so suggestive of liver abscess, was met with four times in some 55 cases investigated for hepatic disorder. In three of the cases, pneumo-hepatography showed a smooth liver contour, and a rounded deformity of the diaphragm. The 'hump' was thus the so-called 'antero-median bulge' caused by a developmental abnormality of the diaphragm. In the fourth case, repeated introduction of air (350 and 400 c.cm.) failed to separate the diaphragm. The 'hump' was unchanged after 15 grains of emetine over five weeks. A week later the case came to autopsy (malignant tertian malaria). The liver appeared normal to the naked eye, and there were no sub-diaphragmatic adhesions on the right side.

Case 6.—Indian male, age 27, admitted with icterus and a tender and slightly enlarged liver. The lower margin of the liver was lobulated, and the spleen palpable. Pneumo-hepatography showed striking foliation of the upper surface of the liver on both sides. The nature of this 'hepar lobatum' was not determined; it was probably coincident with a severe

attack of infective hepatitis, which led to the patient's death (figure 6, A, B, C and D, plate XXV).

Conclusions.—Pneumo-hepatography is a valuable and safe diagnostic aid. It can be used to distinguish between lesions above and below the diaphragm; and by it, alterations in liver contour imposed by deformities of the diaphragm can be separated from those formed by true liver swellings. By it, too, the upper liver contour can be clearly visualized.

We wish to thank Dr. K. R. Paul, assistant medical officer of the Assam Oil Company, and Drs. A. Ahmed, J. M. Kar, and T. Das for their assistance, and the General Manager of the Assam Oil Company for his permission to publish this paper.

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SULPHAMEZATHINE IN THE TREATMENT OF CEREBRO-SPINAL MENINGITIS

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In our previous paper (Karamchandani and Haider, 1945), certain measures were outlined to combat cerebro-spinal fever in this station. These proved to be effective and were applied in the central command. Only 10 cases occurred during the first seven months of 1945, but in all 13 cases were treated with sulphamezathine which was administered as follows:—

Six grammes in 20 c.cm. were given by the intravenous route at once and three further injections of three grammes in 10 c.cm. at six-hourly intervals. After this, the drug was administered orally four tablets (two grammes) every six hours for two days, followed by two tablets (one gramme) six hourly for a day or two more. The time lag between the onset of disease and commencement of treatment was on the average two hours, except in one patient who came 24 hours late and died, and another who came 12 hours late. Five cases out of 13 were received comatose, and all of these were fed through a Ryle's tube. Every case received eight to ten pints of glucose water. Out of 13 cases, one died, i.e. a mortality of 7.7 per cent.

The ages of the ten patients varied from 18 to 25 years. Four cases were seen in January and 3 in April; the rest of the cases were single cases seen in March, June and July.

In our opinion, sulphamezathine is little improvement on sulphapyridine, if the latter

drug is given parenterally as recommended in our paper (Karamchandani and Haider, 1945); moreover, the latter drug can be administered by the intramuscular route as well.

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THE CHEMICAL REACTION OF BLOOD SIMULATED BY GUM

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In an article in this journal (Chakravarti, Roy and Roy, 1944) bearing on this subject, a fallacy in the chemical reaction of blood caused by gum was not mentioned. The present writer wrote to the senior author and sent specimens of gum received from the Stationery Department of the Government of India. The author found most of these samples giving the benzidine reaction of blood and decided to make the necessary correction in his paper. The tragic death of the author a few days ago reminded the writer of the correction which, obviously, had been forgotten.

Gum is known to be a simulator of the benzidine reaction of blood (Grevall and Chandra, 1941). During the recent shortage of tie-on labels, the writer reminded all concerned of the undesirability of sticking labels on medico-legal exhibits with it. The following are the interferences caused by the simulation.

GUM ON STAINS OF DYES OF ANIMAL AND VEGETABLE ORIGIN

Gum added to a cochineal stain on fabric stiffens the latter like a blood stain, and also gives the chemical reaction of blood. In the spectroscopical test, which is the next step in the examination of the stain, the cochineal absorption spectrum does not look much unlike the absorption spectrum of cyanhæmochromogen (Grevall, Roy Chowdhury and Das, 1945).

Stains of some vegetable dyes present similar difficulties.

GUM ON FABRIC AND OTHER EXHIBITS STAINED WITH BLOOD

Dyed fabric.—Vegetable dyes, such as those derived from madder and alkanet root, yield absorption spectra not much unlike those of derivatives of hæmoglobin. In dealing with blood-stained fabric dyed with such dyes (and as a matter of precaution with all unknown dyes), it is essential to examine spectroscopically, as controls, areas which by the chemical test appear free from blood. A smear of gum interferes with the selection of such areas, by giving the false reaction of blood. The chemical tests remaining unfinished, the serological test cannot be applied.

Undyed fabric.—Even in the case of undyed fabric, control from an unstained area is necessary for the antiserum. The gum interferes with the selection of this area also. The serological test cannot be completed.

Weapons, etc.—The unstained areas smeared with gum presents the same difficulties as undyed fabric similarly smeared.

GUM ON STAINS OF BETEL CHEWER'S SALIVA

These stains, which look like blood stains, may pass the chemical test because of a smear of gum. If allowed to slip through the spectroscopical test, they may further simulate the positive serological reaction of blood by precipitating the antiserum by virtue of their high tannin content, due to the catechu and betel-nut in the betel. A weak solution of tannin may not affect the normal serum from an animal, and yet may precipitate an antiserum prepared from the same animal, because the antiserum is richer in globulins than the normal serum. Incidentally, several easily available substances can react likewise: hence the need for a control of the unstained area with the antiserum. This point was not stressed in the early days of medico-legal work in India.

Further, the gum makes stains on fabric stiff to the finger, and stains on weapons soft to the point of the scalpel, and thus simulates also two important physical properties of blood stains.

Here it may be mentioned that the importance of spectroscopy in the examination of blood cannot be overstressed.

With proper care, there is no danger of ever reporting wrongly, and positively on a stain. The care, however, makes it necessary to include many controls for test with many chemicals, with the spectroscope and with several antisera (prepared against several animal proteins). All anomalously-reacting stains are reported as 'disintegrated' for convenience.

The stains of betel chewer's saliva have attracted other workers' attention also (Karunakaran and Vedakkan, paper read before the Indian Science Congress, January 1944).

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PARALYSIS OF NECK MUSCLES IN POLIOMYELITIS

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Introductory

PARALYSIS of one or both legs is the usual legacy of acute anterior poliomyelitis. But the

distribution of the motor loss varies within the widest limits. The paralysis may affect any muscles of the body (Collier, Adie and Walshe, 1941). According to Sheldon (1940), isolated groups of muscles may be involved. Neck muscles often share in ascending or generalized syndromes, but may be involved by themselves (Wilson, 1940). Agius, Bartolo, Coleiro and Seddon (1945) report about their study of 426 cases of poliomyelitis in the Malta epidemic (1942-43). Almost all the cases were in children under the age of five years but none showed paralysis of neck muscles. Bernstein, Clark and Tunbridge (1945) give an account of acute anterior poliomyelitis among service personnel in Malta. The number of cases in this series was 57 but in none among them was involvement of neck muscles.

The appended table (table I) is given by Lovett (1916) for the New York epidemic of 1916.

TABLE I
Distribution of paralysis in 1,166 cases

Group	Number of cases
Both legs	338
One leg	302
Both legs, both arms ..	127
Both legs, one arm ..	101
One arm	83
Homolateral arm and leg ..	38
One arm, one leg opposite ..	29
Both arms	33
Both arms, one leg ..	20
Girdle cases	57
Facial alone	38

Wernstedt's (Wilson, 1940) summary of the distribution of paralysis is tabulated below:—

TABLE II
Summary of paralysis

Localization	Number	Percentage
Leg	4,519	78.6
Arm	2,372	41.3
Trunk	1,601	27.8
Cranial nerve	767	13.3
Throat and neck	333	5.8

From the tables appended above it is clear that paralysis of the neck muscles in poliomyelitis is extremely rare. Below is reported a case of poliomyelitis in which the neck muscles and one arm were involved together.

Case report

N., 2 years, Muslim female child, was admitted to the Children's Ward with the complaints of inability

to hold the neck erect, and diminution of motor power of the right arm, duration 15 days. The onset was after an attack of fever which lasted for 3 days.

On examination.—Temperature, pulse and respiration rates normal. The child could not keep the head erect on the neck. Power to extend the head was totally absent; the head dropped forward, causing a peculiar attitude, which was associated with overaction of the frontalis. The lower cervical spine looked unduly prominent when the head dropped forward. The motor power of the right arm was diminished, and there was loss of biceps and triceps jerks. Sensations could not be tested. There were no fibrillary contractions anywhere in the body. There was no other abnormality anywhere nor in any other system.

Investigation.—Blood: total red cells 4,500,000; total white cells 11,000; haemoglobin 80 per cent; polymorphonuclears 49 per cent; lymphocytes 48 per cent; mononuclears 2 per cent; and eosinophils 1 per cent; W.R. negative. Urine and stool normal. X-ray of the cervical spine revealed no abnormality.

Progress and treatment.—An adequate dosage of vitamins including B₁ and E was given to the child for 2½ months. Gradually the paralysis of neck muscles disappeared and the child could extend the neck, but the paralysis of arm showed no improvement at all, and moreover the arm looked wasted.

Comments

The interest of the case lies in the paralysis affecting the neck muscles which, as pointed out before, is a rare occurrence in poliomyelitis. Out of about 300 cases of poliomyelitis coming under the author's observation during the last 3½ years at Agra, this is the first case in which the neck muscles shared in the paralysis. The muscles involved were the muscles of the back of the neck, the splenius, complexus, etc.

It is difficult to say how far vitamin therapy helped in the disappearance of the paralysis of the neck muscles. The fact that no improvement occurred in the paralysis of the arm stands against the beneficial value of vitamin therapy. The author feels that the regaining of power of the neck muscles probably would have occurred even if no vitamins were given.

My thanks are due to Major-General H. C. Buckley, J.D., F.R.C.S., C.S.I., I.M.S., Principal, Medical College, and Superintendent, Thomason Hospital, Agra, for his kind permission to publish the report of the case.

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INFECTIVE HEPATITIS AMONG INDIANS

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THE cases on which this paper is based were 258 in number. All the cases were treated in hospital during the period 15th May, 1943, to 30th April, 1945. Only those cases have been considered which were admitted from the local Indian units. They were all Indian males. Combatants were admitted in much larger proportions (84 per cent) than non-combatants (16 per cent), though they were all living under similar conditions. The relatively high incidence of infective hepatitis in companies made up largely from reinforcements who had recently undergone vigorous training is striking. For example, during the period of this investigation the I.A.O.C. Depot Battalion had 55 cases in all its companies. The highest number, 18, came from one single company, which on enquiry contained a large number of men who had recently been through vigorous training. In comparison, only 37 cases occurred in all the other five companies. In none of these had the men undergone undue physical strain, being principally composed of one or other of the following categories: leave details, men of low medical category, prisoners and deserters, the unit reception centre and recruits.

Hindus, Muslims, Sikhs and Christians were all affected. The ages of the patients varied from 20 to 45 years, and both fresh recruits and soldiers with long service records were found among our 258 cases. Three officers are also included in the above number.

Symptoms

Patients before admission to hospital had usually complained of 2 to 8 days' moderate fever and then developed yellowness of the conjunctivæ. All grades of jaundice in this region have been observed, from deep to light yellow. In the great majority of cases, the icterus did not disappear during their 3 to 6 weeks' stay in hospital.

A few patients had no pre-icteric fever, but merely suffered from nausea.

Only two patients complained of yellow vision, which had lasted for 2 to 6 days. Bradycardia was commonly observed. A pulse rate of 50 per minute was not uncommon. The most constant symptom was anorexia. Itching of the skin occurred in only one patient. A yellow coloration of the skin could not generally be discerned. Only in one serious case, subsequently fatal, was this obvious. Dark pigmentation of the skin is no doubt the reason for this, as generalized jaundice was very distinctly seen in British soldiers admitted to the British Military Hospital of this station over the same period. The urine was high-coloured and concentrated, and looked like

mustard oil in consistency. Bile pigments and bile salts were found in the urine, if examined at an early phase of the disease. Colourless stools due to lack of bile were not a constant feature.

Total white cell counts ranged between 3,500 and 8,600 with differential counts as follows:—

	Per cent
Polymorphs	47 to 75
Lymphocytes	20 to 45
Mononuclears	2 to 4
Eosinophils	2 to 14
Basophils	1

Patients were not anæmic, nor were they undernourished. Tenderness of the hepatic region was more common than enlargement of the liver. The spleen was palpable in a few cases only. Nearly all the patients remained apyrexial during their stay in hospital.

Diagnosis

In the case of icterus due to anæmia, hæmoglobin estimations and white cell counts gave the clue, and the appropriate treatment was instituted. If stools were found positive for ova of intestinal parasites, deworming was carried out guardedly. Icterus in such cases improved rapidly. Icterus in cases of hæmoglobinuria and blackwater fever was encountered, and appropriate treatment was given. Four cases gave a history of previous treatment with arsenical injections on account of syphilis. Infective hepatitis was diagnosed only in the presence of conjunctival icterus, bradycardia, anorexia, tenderness in the hepatic area, high-coloured urine with or without the presence of bile pigments and bile salts. If the stools were light-coloured, this further supported the diagnosis.

General

All patients suffering from infective hepatitis were isolated, and were permitted to use only their own sanitary annexe. All dejecta were disinfected with 2½ per cent cresol before disposal. Patients were given a generous high carbohydrate and protein diet, with extra sugar and fresh limes. Fats were restricted only in the case of patients with light-coloured stools. All patients gained in weight during their 3 to 6 weeks' stay in the hospital. On their discharge they were recommended one month sick leave in their homes.

The following are the notes of a fatal case observed in this series:—

A sepoy fitter, a Christian, aged 27 years, was admitted into hospital on 3rd March, 1945. He had complained of anorexia, weakness, yellow coloration of the eyes and of passing white-coloured stools.

The duration of the illness was 7 days. Previously he had suffered from malaria and dysentery.

The pulse rate was 70 per minute. Other systems were normal. The patient ran an intermittent temperature, up to 101°F. This settled down in a week but relapsed again a little later. Stools showed no ova and cysts. Bile salts were found in the urine. Despite repeatedly negative blood slides, clinical malaria was

suspected and mépacrine (0.1 gm. t.d.s.) was administered from 19th March to 25th March.

On the 25th March, the patient became unconscious. The conjunctivæ appeared deeply icteric, and the pupils were widely dilated and reacted sluggishly to light. The left knee-jerk was present, but the right knee-jerk absent. Plantar reflex was flexor on the left and extensor on the right. Temperature was normal, pulse rate 72 per minute with a good volume and regular rhythm.

On the 26th March, the pulse rate fell to 60 per minute, respirations were 20 per minute, and sphincter control was lost. The lungs were clear on auscultation, and there was no abdominal rigidity. Lumbar puncture was carried out, revealing a clear yellow-coloured fluid, which was slightly under pressure. The urine contained no albumin or acetone, but turned an opalescent green with Benedict's solution.

Blood examination gave a hæmoglobin value of 14.5 grammes per cent; total red cell count of 5,440,000 per c.mm.; total white cell count 6,600 per c.mm.; differential count: polymorphs 75 per cent, lymphocytes 20 per cent, mononuclears 2 per cent, eosinophils 2 per cent, and basophils 1 per cent. Poikilocytosis and normoblasts were absent.

On the 27th March, acute dyspnoea, clonic spasms and cyanosis developed. Glucose and saline were given intravenously also by mouth, and oxygen, but the patient died that evening. Post mortem was performed by the officer in charge of the District Laboratory on the 28th March, 1945, who gives the following report:—

General.—Skin looks lemon tinged. Chest—muscles emaciated. Subcutaneous tissue bile tinged. Heart—small and globular, devoid of fat, thick walled. Weight 9½ oz. Valves and coronaries show no defect. Petechial hæmorrhage in the pericardium and myocardium present. Lungs—no abnormality detected. Abdomen—little fat in the wall or over the peritoneum, it is bile tinged. Stomach and intestines show no ulceration, but scattered areas of petechial hæmorrhage are noted. Spleen—soft, and on cutting, the malpighian bodies are prominent and confluent. Liver—reduced in size, capsule somewhat wrinkled and the organ is flattened out when placed on a table. Surface is pale in colour, with a few yellowish white patches here and there. No tubercles are seen. The organ can easily be bent double on its base. On cutting, the normal pattern is lost, and it shows large dirty-yellow areas intermingled with dark brown areas. Weight of the liver is 32 oz. (normal 50 oz.). Gall-bladder and bile duct show no calculi or abnormality. Abdominal glands are slightly enlarged and inflamed, but on cutting show no fibrosis or caseation. Pancreas—normal. Kidneys—lobulated, deeply congested and show hardly any demarcation of the cortex from the medulla. Skull—brain surface markedly congested. Weight 50 oz. Meninges—clear and non-adherent. No increase of fluid in the ventricles.

Histopathology. Brain—congested with dilatation of sinuses and increase in endothelioid cells. Heart—no pathological changes. Kidneys—cloudy swelling of the tubules and swelling of the glomerular tufts, almost filling the Bowman's capsules. Hæmoglobin pigment is scattered all over in small quantity. Liver—total degeneration of the individual cells of the parenchyma apparent. There is no liver pattern seen anywhere. Spleen—slight congestion only.

Opinion: A case of cholæmia following acute atrophy of liver.

This fatal case serves as a warning that infective hepatitis can always develop into a serious condition.

Patients should therefore be kept in bed so long as their stools remain pale and they feel depressed.

Drugs having a possible deleterious effect on the liver cells should be avoided if possible.

Arsenic is contra-indicated; deworming should be postponed and anti-malarial drugs, such as mepacrine and plasmoquine, also avoided if possible.

No reliance can be placed on the icteric tinge of the eyes in deciding the prognosis.

General treatment.—The routine treatment carried out in our hospital was magnesium sulphate $\frac{1}{2}$ ounce, every morning, sodium salicylate three grains thrice daily and calcium lactate ten grains thrice daily.

(Medical officers, sisters and other nursing personnel were encouraged to adopt a judicious but unconcerned attitude towards these patients. For it was observed that when too vigorous a line of treatment or laboratory examination was undertaken, it affected the patients' morale, and convalescence was retarded.)

Summary.—Infective hepatitis is not an uncommon disease among Indians, and diagnosis is comparatively easy.

Of the 258 cases admitted during the two years, 84 per cent were combatants and the rest non-combatants.

Those who had undergone severe physical training were more prone to suffer from infective hepatitis.

The maximum number of cases occurred during the month of September.

If treated in a routine manner, recovery is complete.

Out of 1,500 cases which have been invalided out of the Army from this hospital, not one was on account of infective hepatitis.

Two cases proved fatal. The complete post-mortem report of one case is given. Gross lesions were seen in the liver cells, which leads one to think that the disease should not be treated lightly in spite of mild outward symptoms.

I thank Lieut.-Colonel H. M. Salamat Ullah, M.C., I.M.S./I.A.M.C., Officer Commanding this hospital, for kindly placing all the hospital records at my disposal and for according permission to publish this paper. I am indebted also to Brigadier B. E. Schlesinger, Consulting Physician, Central Command, India Command for making valuable suggestions and corrections.

THE TREATMENT OF KALA-AZAR WITH SODIUM ANTIMONY-V-GLUCONATE: PRELIMINARY OBSERVATIONS*

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A PENTAVALENT antimony compound (Sdt. 561, solustibosan, antimony-v-hexonate, con-

taining 20 mg. of antimony per c.cm. of solution), that made a stable solution and could be given intramuscularly, was first introduced by Prof. H. Schmidt, the pioneer worker on pentavalent antimony compounds. Kikuth and Schmidt (1938) found that this compound possessed a marked curative action in the leishmaniasis of hamsters. Napier *et al.* (1937) first tried this drug in the treatment of ten cases of Indian kala-azar, with successful immediate results. Ultimately it was considered that though the drug possessed considerable anti-kala-azar activity, it was less efficacious than the older compounds of p-aminophenyl stibinic acid, e.g. neostibosan (Napier, 1943).

After the outbreak of the World War II, a British equivalent of solustibosan, viz, sodium antimony-v-gluconate, was produced, and the drug was tested in a small series of cases of kala-azar in 1942, with none too successful results. This led to a statement in the paper on the treatment of kala-azar with pentamidine, M&B 800 (Napier and Sen Gupta, 1943), '... the drug (sodium antimony-v-gluconate) cannot be regarded as possessing anti-kala-azar activity comparable to neostibosan and urea stibamine . . .'. This statement Burke and Chakravarty (1944) criticized adversely in their report on treatment of 21 cases of kala-azar with this drug. The total dosage adopted by Burke and Chakravarty was 60 c.c. of the solution per 8 stone, i.e. 112 pound, body-weight. They reported that this was adequate to cure kala-azar in Assam and were quite effusive in their praise of the drug, though they reported only the immediate results of treatment.

Actually in this institution in 1942, a total of 9 cases, of which 7 cases referred to in the paper on pentamidine, had been treated with sodium antimony-v-gluconate. Of these 9 cases, there was marked improvement without permanent cure in 4 cases; slight improvement in two cases; the drug was quite ineffective in one case, and in two cases clinical recovery that was probably permanent was seen. All the cases, except these two, required further anti-kala-azar treatment with other pentavalent antimonials or aromatic diamidines for their complete cure. The drug was tried in a dosage scheme devised on the assumption that it should be calculated on the basis of the antimony content, and that it should be similar to that of the other pentavalent antimony compounds, so that 1 c.c. of sodium antimony-v-gluconate was regarded as equivalent to 1 c.c. of 5 per cent solution (or 0.05 gm.) of neostibosan.

The table gives the dosage adopted in these cases.

Only the cases 5 and 6 showed cure. The remaining seven patients who did not make a complete recovery had more than 60 c.c. per 112 lb. body-weight excepting patient no. 7 who had only 58.02 c.c. The results were thus quite unsatisfactory, and justified the statement referred to above. The results in the

*The work reported in this paper was undertaken under the Endowment Fund of the Calcutta School of Tropical Medicine, aided by a grant from the Indian Research Fund Association.

TABLE

Case number	1	2	3	4	5	6	7	8	9
Weight (lb.)	78	24	32	60	18	19	83	75	22
Total dose (c.c.)	52	27	38	36	30	81.5	43	54	25
Total dose per 112 lb. body-weight in c.c.	74.6	126	133	67.2	186.6	480.4	58.02	80.6	127.2

present series are considerably better, but we still have to demonstrate that the relapse rate is comparable to that seen with the older pentavalent antimonials before the drug can be recommended for wide adoption.

The dosage scheme adopted in the early trials of the drug solustibosan and sodium antimony-v-gluconate did not take into account certain pharmacological factors concerning its toxicity and its excretion. Napier *et al.* (*loc. cit.*) and Weese (1937) found that the toxicity of solustibosan was very low; 18.5 c.c. or 370 mg. Sb. in the mouse (Napier *et al.*) and 20 c.c. or 400 mg. of Sb. in the rabbit (Weese, *loc. cit.*) per kilo body-weight was the lethal dose, the corresponding lethal dose for neostibosan being 0.3 gm. containing 126 mg. of Sb. per kilo body-weight and 0.5 gm. = 210 mg. of Sb. for the mice and the rabbit respectively. Thus, gramme for gramme of antimony, solustibosan was markedly less toxic than neostibosan. Also Weese (*loc. cit.*), and Goodwin and Page (1943) found that about 80 per cent of this drug was excreted within the first twenty-four hours. Boyd and Ray (1929) had found that, after the intravenous administration of neostibosan, the excretion during the first twenty-four hours amounted to 41 per cent, and during the next twenty-four hours to 6 per cent; during the next few days the residue was excreted very slowly.

These findings suggested that much larger doses (larger when calculated on the basis of Sb. content) of solustibosan or sodium antimony-v-gluconate would be tolerated, and that it was necessary to repeat the injections at relatively short intervals in order to maintain any level of the drug in the body. It had been found by Kentenich (1937) that 400 to 480 c.c. of solustibosan as the total dose was readily tolerated by patients suffering from multiple sclerosis. It thus came to be realized that single doses of 15 to 20 c.c. of sodium antimony-v-gluconate would be readily tolerated, and that the injections should preferably be given on consecutive days. Patel (1944) treated a series of 6 cases with this drug using 15 to 20 c.c. as the single dose and 180 to 200 c.c. as the total dose. All his cases were completely cured. Burke *et al.* (*loc. cit.*) used the total dose of 150 c.c. in a few of their cases of kala-azar, the course being 10 injections of 15 c.c. each. Also a concentrated solustibosan containing 100 mg. of Sb. per c.c. has been used with success in the treatment of Mediter-

ranean kala-azar (Lozano Morales, 1943; Kikuth and Schmidt, 1943), and a Russian equivalent of the same drug was used with success in the treatment of kala-azar in the U.S.S.R. (Kornetov and Mirzoyan, 1942).

About the beginning of this year, it was decided to give another therapeutic trial to the drug sodium antimony-v-gluconate, using large single doses of 15 to 20 c.c. in adults, and giving the injections on consecutive days. Up till now, 50 cases of kala-azar and two cases of post-kala-azar dermal leishmaniasis have been treated with this drug, and in this paper it is proposed to present the preliminary results of this trial.

The patients

All the patients, except two treated as out-patients, were admitted under the care of the senior author into the Carmichael Hospital for Tropical Diseases.

Of the 50 cases of kala-azar, 46 were in Indians, 3 in Anglo-Indians, and one was in a Jew; 38 patients were males and 12 females.

The age distribution was as follows:—

1 to 10 years	16 patients
11 to 20 "	16 "
21 to 30 "	10 "
31 to 40 "	4 "
Over 40 "	4 "

Diagnosis

The diagnosis of kala-azar was confirmed in all the cases, except three, by the demonstration of the *Leishmania donovani* in the sternal, splenic or tibial puncture smear. In two of these three cases, the diagnosis was confirmed by the positive aldehyde, antimony, and the complement-fixation tests for kala-azar; the third was an aldehyde-test-positive case with cancrum oris.

The aldehyde test was done in 47 cases, it was positive (+++, ++, or +) in 25 cases, doubtful [(+), ±] in 7 cases and negative in 15 cases. The complement-fixation test was done according to a modified technique described by the senior writer (Sen Gupta, 1945), in 49 cases; a 'strongly positive' reaction was obtained in 23 cases, 'positive' in 22, 'doubtful' in one, and negative in 3 cases (i.e. approximately 92 per cent positive). One of the three cases showing a negative reaction and that showing a doubtful reaction were complicated by cancrum oris (see Sen Gupta and Chakravarty, 1945).

Blood picture before treatment

The hæmoglobin values of the series of cases yielded a mean of 8.02 gm. per 100 c.c. of blood with a standard deviation of ± 2.54 gm. The leucocyte counts showed a mean of 3.69 ± 1.95 thousand per c.mm. of blood.

Treatment

Sodium antimony-v-gluconate was the only 'specific' drug used. The injections were given intramuscularly on consecutive days, ten to twelve days in a course in most cases. In others the number varied from 9 to 14. The maximum individual dose varied according to the age and the weight of the patients; the adults usually received 15 to 20 c.c. of the drug and the children 6 to 15 c.c. according to the age. The intramuscular injections of the drug were well tolerated by the patients, and an out-patient could walk home without any difficulty 15 to 20 minutes after receiving an injection of 20 c.c. of the drug in the gluteal muscles.

Seven patients, including 2 cases with relapse after previous antimony treatment, required two courses of injections. Besides the specific treatment, symptomatic treatment was adopted for the complications, e.g. cancrum oris, hæmorrhages, dysentery, diarrhoea, respiratory infections, jaundice, etc., when present. Subsidiary treatment for latent malarial infection, hookworm or other helminthic infections and for anæmia was carried out when necessary, either during the stay of the patient in the hospital or at the out-patients department after the patient had been discharged from the hospital soon after the completion of the specific treatment.

Results of treatment

General.—Forty-eight out of 50 patients made clinical recovery; 42 after one course of injection and 6 after two courses; 2 died.

Fever.—Usually the fever came down to normal after four to five injections. Except in a resistant case which required two courses of injections before becoming afebrile, all patients became apyrexial after the completion of the first course of injections.

Spleen.—A decrease of the size of the spleen was noticed quite early in most of the cases. At the end of the course of injections in almost all cases the spleen showed signs of reduction in size.

A fortnight after the completion of the treatment, in the cases with splenic enlargement up to 4 inches, the spleen was either not palpable or only slightly enlarged, and readily replaceable under the costal margin. In the cases with more marked splenic enlargement too, a considerable diminution in size was apparent.

Blood picture after treatment

A second blood count was done a fortnight after the completion of the specific treatment in all cases in which it was possible. In all, 39 cases had a second blood count done a fortnight after the completion of the specific treatment. The mean hæmoglobin content per 100 c.c. of blood was 10.71 ± 1.60 gm. and the mean leucocyte count 8.01 ± 2.29 thousand per c.mm. of blood. Both the values indicate a significant rise above the corresponding figures obtained before treatment.

Improvement in other clinical features

Improvement of the general condition was noticeable quite early during the first course of injections in all cases, and was seen simultaneously with the cessation of fever. In the cases with cedema there was an initial loss of weight due to loss of cedema. In others (the majority of cases) there was a progressive increase of weight.

Failures

In two cases the drug was unsuccessful in leading to a clinical cure. One of these cases had agranulocytosis complicating kala-azar, a very fatal combination; and the other failed to respond at all to all treatment, specific and symptomatic, for his various ailments. The notes of these cases are reported below:—

Case 1.—G. G., an Indian boy aged 10 years, was admitted on the 28th May, 1945, for irregular fever without chill and rigor for three months, emaciation and weakness, and bleeding from the gums for one month. On admission the patient was found to be very weak and anæmic and emaciated. Temperature— 102°F. , pulse/respiration—138/36. Heart—no abnormality except tachycardia. Lungs—signs of bronchitis. Liver—just palpable. Spleen—enlarged $3\frac{1}{2}$ inches below the 9th rib.

Laboratory investigations. Urine—no abnormality; stools—hookworm and ascaris ova; aldehyde, antimony and complement-fixation tests—positive.

Blood counts.—These are shown in the following table.

Date	Hb. gm., per cent	R.B.C. in million	MCV	MCH	MCHC	W.B.C. in thousands	N.	L.	M.	E.	Plasma cell
29th May ..	5.91	2.34	91.8	25.2	27.7	1.6	2	59	38	0	1
30th May	1.1	1	54	44	0	1
1st June	1.0	0	60	40	0	0
2nd June	1.1	0	58	39	0	3

Agranulocytosis was thus seen before any treatment was given. On 29th May, 1945, it was found that the patient had high fever of 104°F. and was looking very ill. Some purulent blisters surrounded by a zone of erythema had developed over the chin and over the abdomen. The tongue was not sore and the patient had no difficulty in swallowing. Pulse/respiration—144/40 per minute. Blood count showed agranulocytosis. The patient was put on penicillin 20,000 units intramuscularly every three hours, sodium antimony-v-gluconate intramuscularly, liver extract parenterally besides various supportive treatment. Pentnucleotide was not available. During the next two days the purulent blisters, which had yielded a pure growth of *Staphylococcus aureus*, subsided, but the general condition did not show any improvement. Signs of peripheral circulatory failure developed on the 31st May, and the condition did not respond to serum transfusion, suprarenal cortical extract, and various therapeutic measures. The patient died on the 4th June, 1945.

This is probably the second recorded case of untreated Indian kala-azar complicated by agranulocytosis, the first being reported by Das Gupta and Sen Gupta (1943).

Case 2.—R., an Indian male aged 25 years, a 'desitute' patient, was admitted on the 17th May, 1945, for oedema of the legs for ten days, progressive weakness and emaciation for six months. He did not give any history of fever during the preceding six months. The patient was found to be very weak and anæmic, with oedema of the legs. Heart and lungs—no abnormality. Liver—not enlarged. Spleen—enlarged up to 1½ inches.

On routine tests it was found that the aldehyde, antimony and complement-fixation tests for kala-azar were positive, and a sternal puncture showed Leishman-Donovan bodies. Blood count showed hypochromic anæmia, with Hb. 7.28 gm. per cent, and W.B.C. 3,875 per c.mm. Stools showed hookworm and ascaris ova, and the urine no abnormality.

The patient was treated for anæmia with ferrous sulphate, and for kala-azar with sodium antimony-v-gluconate, 210 c.c. in 11 injections. The oedema subsided within a few days and the patient felt considerably better; the splenic enlargement was somewhat less at the completion of the specific treatment for kala-azar. But the blood picture did not show any improvement. He was given a second course of sodium antimony-v-gluconate, treatment for the helminthic infection, quinine for any latent malaria, anti-anæmic drugs but without producing any appreciable improvement. The patient gradually grew more and more asthenic and ultimately died on the 4th July, 1945.

Discussion

Of the fifty cases of kala-azar treated with sodium antimony-v-gluconate, 48 cases fulfilled the criteria of immediate clinical cure, viz, they became apyrexial, the size of the spleen showed well-marked decrease, the general health improved, and the blood count showed well-marked improvement. Two patients died. The immediate cure rate was thus 96 per cent, this figure is quite comparable to those obtained with pentavalent antimony compounds in general by Napier (1932).

Analysis of the dosage employed shows that the total dosage of sodium antimony-v-gluconate (20 mg. Sb. per c.c.) in one course of in-

jections, to produce a clinical cure, was as follows:—

Class of patients	Mean total dose in c.c. \pm s.d.	Relative total dose per 100 lb. body-weight in c.c. \pm s.d.
Adults, age 15 or above; weight over 60 lb.	181.8 \pm 25.2	208.6 \pm 34.2
Adolescents, age 10-14, weight 40 to 60 lb.	127.5 \pm 28.9	272.9 \pm 64.8
Children, age below 10, weight below 40 lb.	93.7 \pm 23.2	369.7 \pm 111.1

This shows that relative to the body-weight, much higher doses are tolerated and required for a clinical cure by adolescents and children, than by adults.

With the help of the above table, the average total dose required for a course can be readily calculated as follows for the above three groups:—

Children	..	3.7 c.c. per pound body-weight.
Adolescents	..	2.7 " " " "
Adults	..	2.1 " " " "

Or roughly, 4 c.c. for children, 3 c.c. for adolescents, and 2 c.c. for adults per pound of body. These figures refer to the drug sodium antimony-v-gluconate, containing 20 mg. of metallic antimony per c.c.; injections being given on consecutive days for ten to twelve days. For adults it is preferable not to exceed a total dose of 220 to 230 c.c. in a course. The individual doses should not exceed 20 c.c. for an adult, 15 c.c. for an adolescent, and 10 c.c. for a child. It is preferable to commence with a small initial dose just to test whether the patient is sensitive to antimony or not.

The course of injections may have to be repeated if the patient does not show evidence of clinical cure within a fortnight of the completion of a course of specific treatment.

The question of permanent cure

That the immediate results are not a very reliable indication of a permanent cure is well recognized (Napier and Sen Gupta, *loc. cit.*; Sen Gupta, 1944). There is needed a follow-up of the clinically cured cases six months or more after the completion of the specific treatment; this study of these cases will form the subject of a future publication.

Post-kala-azar dermal leishmaniasis

Two cases, in Indian male adults, of post-kala-azar dermal leishmaniasis (one with 'peri-onychia induration' type of lesions, and the other with extensive depigmented patches, erythema, and multiple nodular lesions superficially resembling oriental sore) were treated with this drug. They were given two courses of 10 to 11 injections at the interval of a week. There was early and marked improvement of

the skin lesions in both the cases. The cases will be followed up to find out the final results.

Summary

1. The available literature regarding anti-mony-v-hexonate (solustibosan) and its British and other equivalents has been reviewed, and the rationale of the adoption of a dose much higher than that used in the early trials discussed.

2. A series of 50 cases of Indian kala-azar and two cases post-kala-azar dermal leishmaniasis was treated with sodium antimony-v-gluconate.

3. Forty-eight cases of kala-azar showed evidences of immediate clinical cure. Of the two fatal cases, one had agranulocytosis. This is the second recorded case of Indian kala-azar showing this complication. Both the cases of post-kala-azar dermal leishmaniasis showed rapid and well-marked improvement.

4. The immediate cure rate in this series (96 per cent) is closely comparable to that obtained with the best of the pentavalent antimony compounds.

5. A scheme of dosage for the different age groups and types of cases has been worked out.

6. Until the relapse rate has been studied, accurate evaluation of this drug in kala-azar is not possible.

Acknowledgment

Our thanks are due to The Glaxo Laboratories Ltd. and their representatives in Bombay and Calcutta for the generous supply of sodium antimony-v-gluconate with which this trial has been carried out. This compound is now marketed under the name of stibatin.

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Later note.—So far, out of the 48 cases of recovery under stibatin treatment, here recorded, five cases have relapsed. The period of observation of most of the cases is still less than 6 months, and further relapses are possible. A note on this subject will be published later.—P. C. S. G.

'PARENTERIC' FEVER DUE TO BACT. FAECALIS ALKALIGENES

A CLINICAL STUDY WITH CASE REPORTS

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Bacterium faecalis alkaligenes, though almost a constant inhabitant of human intestines (Topley and Wilson, 1936), may play a pathogenic rôle in certain conditions, giving rise to clinical states resembling enteric group of fevers (Petruschky, 1896; Hirst, 1917). Four such cases are reported here.

1. A sepoy, aged 30, had fever for 3 days prior to admission and was passing diarrhoeic stools. On admission, the patient was of slow disposition, with a slightly toxic look; tongue furred; respiration 20; pulse 32; distinct tenderness over the liver region especially over the gall-bladder. No other abnormality found on clinical examination. The patient had two bouts of diarrhoea lasting two to three days during his illness. There were evening rises of fever which lasted 21 days (figure 1).

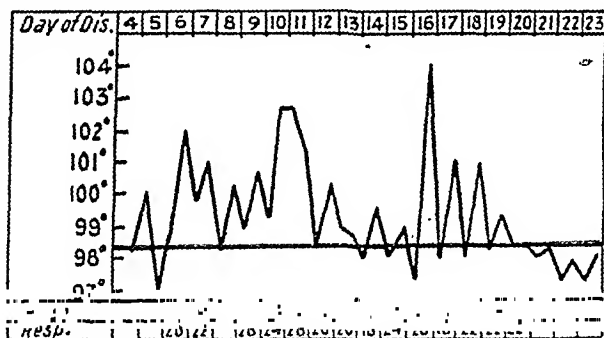


Fig. 1.

Malaria parasites (*falciparum*) were found in blood films and the patient was put on routine anti-malarial treatment but without any response. Amoebic hepatitis was suspected, but a course of emetine elicited no response. Otherwise the patient was treated on symptomatic lines and made a complete recovery.

Laboratory investigations.—Agglutination tests for typhus, typhoid and abortus fevers gave negative results. Total W.B.C. 11,600; differential count—polymorphs 70 per cent, lymphocytes 18 per cent, monocytes 12 per cent, haemoglobin 13 gm. Aldehyde and antimony tests were negative. Sternal puncture showed no Leishman-Donovan bodies. From blood culture *Bact. faecalis alkaligenes* was isolated and the serum

agglutinated the organism to a titre of 1 : 150. Stool on routine examination showed only ova of round worms. Urine normal. X-ray of the lungs showed no abnormality.

2. A civilian labourer, aged 20, admitted with fever and rigor, duration 4 days; spleen enlarged 3 fingers; liver slightly tender but not palpable; heart and lungs clear. Blood films showed no malaria parasites; nothing else abnormal detected. On the 7th day the patient passed tarry urine, which was found to be due to hæmoglobinuria. In view of the enlarged spleen the patient was given treatment for blackwater fever, viz, alkalis, intravenous salines and mepacrine. The hæmoglobinuria stopped in 24 hours, but a daily rise of temperature continued for 36 days (figure 2).

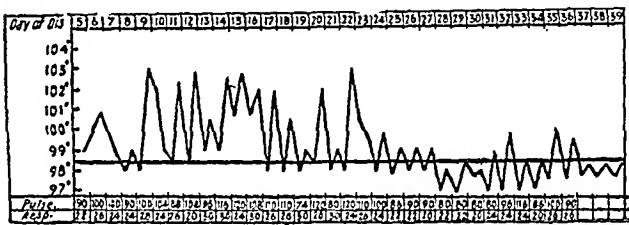


Fig. 2.

Toxæmia was slight; there was no diarrhœa or clinical anæmia.

Laboratory investigations.—Blood culture showed *Bact. fæcalis alkaligenes*. W.B.C. rose from 10,000 to 21,000 on the 17th day and gradually fell to normal in four weeks; stool and urine showed no abnormality, and their repeated cultures showed no pathogens; Widal and Weil-Felix tests were negative; Kahn test was first positive and later negative. Sternal smear showed no Leishman-Donovan bodies; its culture was sterile. There was hyperplasia of the erythropoietic tissue, but proliferation proceeding at a normal rate. Results of direct agglutination against the isolated organisms were : 19th day 1 in 1,500, 33rd day 1 in 160, 47th day from the beginning of the illness 1 in 50.

Hæmoglobinuria appears to be only an associated condition due to blackwater fever. The positive Kahn test raised the question of paroxysmal hæmoglobinuria, but this was excluded by a negative Rosenbach's test. The patient was treated symptomatically and had an uneventful recovery.

3. A civilian labourer, aged 20, admitted for fever with rigors and pain in joints, duration 3 days. No abnormality detected clinically except slight tenderness over the liver. Fever lasted for 11 days, and was remittent in type till it fell by crisis (figure 3).

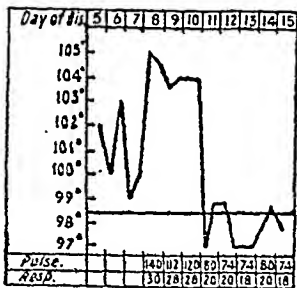


Fig. 3.

Blood films showed B.T. rings, but the fever showed no response to anti-malarial treatment, and the patient made an uneventful recovery on symptomatic treatment.

Blood culture showed *Bact. fæcalis alkaligenes*; direct agglutination against the organism was 1 in 50, 16 days after the fall of temperature. Stool and urine were normal on culture and routine examinations.

4. A civilian labourer, aged 37, admitted for fever with rigor for 3 days; bowels constipated; spleen and

liver not palpable; heart normal; lungs showed a few scattered râles and no consolidation. The patient was somewhat toxæmic but complained of no serious discomfort despite fever, which was remittent and later intermittent, often showing a double-spiked pattern as found in kala-azar. There was no rigor associated with fever which lasted for 55 days (figure 4).

Laboratory investigations.—Weil-Felix and Widal tests were repeatedly negative; total W.B.C. was 7,200 and, later 4,250; blood culture showed *Bact. fæcalis alkaligenes*, and the patient's serum agglutinated the organism to a titre of 1 in 250; sputum showed no acid-fast bacilli; urine and stool were normal on routine examinations and their culture revealed no pathogens. Aldehyde and antimony tests were positive; sternal puncture showed Leishman-Donovan bodies; x-ray of the chest was normal. Patient was treated on purely symptomatic lines and the temperature came down to normal with a course of urea-stibamine.

Discussion

The pathogenicity of *Bact. fæcalis alkaligenes* in causing an enteric-like clinical syndrome was first shown by Shearman and Moorhead (1916) in routine blood culture in Egypt in the last war. Subsequently Hirst isolated *Bact. fæcalis alkaligenes* in no less than 23 times out of a total of 133 positive blood cultures (18.7 per cent).

This organism frequently gains entrance into the system through the intestinal mucosa damaged by enteric fevers and dysenteries. Hirst carefully examined 100 consecutive stools, after preliminary purge, of patients convalescent after enteric fever and dysenteries and those of apparently normal persons who gave no definite history of diarrhœa, etc., in the previous ten months, and found that *Bact. fæcalis alkaligenes* was present in a large proportion of stools of those convalescent after gastro-intestinal disturbances.

	Total	<i>Bact. fæcalis alkaligenes</i> found.
Enteric convalescents ..	43	16
Dysentery ..	57	29
Normal stools ..	60	Nil

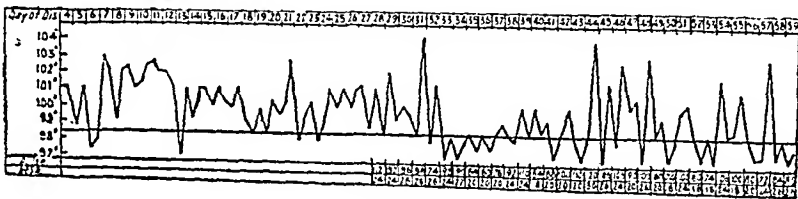


Fig. 4.

A higher incidence of parenteric fevers (as the name suggested by Chaudhuri, 1944) may be expected naturally in tropical countries like India and Egypt, where factors which damage intestinal mucosa are legion. Even in cases where direct association with intestinal diseases cannot be traced, lesions due to amœbæ, patho-

genic protozoa, and diet, containing strong condiments, agreeable to the palate but harmful to the mucosal lining, may be present, causing slight or even inappreciable symptoms. Thus, the possibility of parenteric fever should always be borne in mind in the pyrexias of unexplained origin in the tropics.

With increased T.A.B. inoculations in the population, especially in the Army, irregular fevers due to septicæmias caused by organisms such as *Bact. fæcalis alkaligenes* are more likely to be met with, and the necessity of repeated hæmocultures and agglutination tests cannot be overemphasized.

It is noticeable that there is no specific character of the temperature charts, which may vary from typical typhoid-fever like to complete irregularity. The duration of the fever varies from two to five weeks. The temperature ultimately comes down to normal due to the production of immune bodies, as shown by raised agglutination titres in all genuine cases. These, and not the alkalis administered, would possibly explain the cure of cystitis caused by *Bact. fæcalis alkaligenes* in the case described by Ahad (1942), who discussed the cultural reactions of the organism and also reviewed the literature.

A note of caution may, however, be sounded in diagnosing this disease, for *Bact. fæcalis alkaligenes* may also be a contaminant in blood cultures.

Diagnosis depends upon.—(i) Isolation of the organism from blood, but its mere isolation is not a proof of its pathogenicity.

(ii) Direct agglutination, as far as possible, with a standardized suspension of the isolated organism is essential as there are no less than 134 strains of this bacillus (Topley and Wilson, 1936). An agglutination titre of 1 in 50 and above is diagnostic.

The writer had to ignore positive blood cultures in no less than eight cases which had not strictly conformed to this criterion. Incidentally, the pathologist must ask for the patient's serum before discarding the culture, which he is apt to throw away after reporting its isolation.

(iii) *Clinically.*—There is irregular fever and slight toxæmia. There is generally a mild leucocytosis with possible slight increase in monocytes; some tenderness over the liver is often present; there may be diarrhoea. In uncomplicated cases, the patient makes an uneventful recovery, though a fatal case with delirium, meningeal symptoms, and terminal broncho-pneumonia, has been described by Chaudhuri.

Of the 41 cases described in literature including those in the present article, and those of Straub and Krause, Roehaix and Marotte referred to by Hirst, the associated diseases and precipitating causes of this septicæmia were not

only variable, but also may not be detected at all, as shown by the following table:—

Preceded by diarrhoea and vague abdominal discomfort	18
Following or mixed with dysentery and enteric fevers	6
Derived from abscess	1
Associated with cystitis	1
Associated with kala-azar	1
Associated with blackwater fever	13
No "appreciable" causes	41
TOTAL	—

The term 'parenteric fever' suggested by Chaudhuri is a convenient one to denote blood invasion by intestinal bacteria, but should only be used, as far as possible, by qualifying with the offending organism.

Summary.

1. Clinical manifestations of parenteric fever due to *Bact. fæcalis alkaligenes* have been described with descriptions of 4 new cases.
2. It is emphasized that diagnosis depends upon isolation of the organism from blood, but the only reliable proof of its pathogenicity is direct agglutination with the patient's serum, for which co-operation between the physician and the pathologist is necessary.

Acknowledgments

Thankful acknowledgments are due to Lieut.-Colonel J. W. Lusk, I.A.M.C., for encouragement and suggestions, and to Colonel W. McAdam, O.C., I.G.H. (I.T.), for permission to report the cases. Acknowledgments are also due to Captain H. M. Rice, R.A.M.C., and Major J. C. S. Paterson, R.A.M.C., for criticism and laboratory investigations.

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We comment on two points in this paper; (1) The fourth case here recorded is strange in several ways.

The fever was of three days' duration (but no statement is made regarding previous febrile periods) and the spleen was not palpably enlarged. The clinical picture however was that of kala-azar. The antimony and aldehyde tests gave positive results and sternal puncture showed *Leishmania donovani*. The fever responded to urea-stibamine.

The aldehyde and antimony tests become positive as a rule only after several weeks' fever and only when the spleen has become considerably enlarged. It is usually impossible to demonstrate Leishman-Donovan bodies on the 4th day of kala-azar fever.

Although the reported findings are anomalous, the finding of Leishman-Donovan bodies and the response to antimony makes one accept the diagnosis of kala-azar. But why the diagnosis of parenteric fever due to *Bact. fæcalis alkaligenes*? The author states that

'mere isolation from the blood is not proof of pathogenicity' of this organism. We presume that the author regards the 1 in 250 agglutination of the patient's own organisms with his own serum as proof in this case. Is this conclusive?

(2) We do not feel very happy about the use of the term 'parenteric' for fevers of this group.

The term 'enteric fever' is used by British authors for the fevers of the typhoid group including typhoid and the para-typhoid fevers. The word enteric simply means pertaining to the intestine, and its use for this group of fevers, while open to objection, is sanctioned by use in British medical literature, but not apparently in American, for Dorland's medical dictionary does not even mention 'enteric fever' or the 'enteric' group of fevers.

It is perhaps not wise to introduce the term 'parenteric' for a fever which shows some resemblances to the fevers of the typhoid group, but which is really a septicæmia with little relation to the intestine (enteron).—EDITOR, I.M.G.

ON THREE CASES OF IDIOSYNCRATIC URTICARIA IN COURSE OF RELAPSING MALARIA

By STEFANINI MARIO, M.D. (Rome)

A RECENT report by Sen Gupta (1942) has renewed interest on some idiosyncratic reactions occurring in man in the course of malarial infestation. Workers from different parts of the world have already reported clinical conditions believed to be due to hypersensitiveness in course of malaria infestation.

Sen Gupta (1942), summing up the current opinion of different workers on the subject, thinks that the symptoms of idiosyncrasy in the course of a malaria infestation are due to hypersensitiveness to the malaria parasites or products of the destruction of the red blood cells; that would explain why the symptoms of idiosyncrasy usually appeared at the onset of the malarial paroxysms and never, so far, in clinically fresh cases.

Case 1.—P. L., male, aged 30, admitted under my care on 17th June, 1942. Malaria (vivax) in 1940 (Lower Sudan). Typical attack of malaria fever with acute pain in the right iliac fossa in the afternoon of the 16th. The rise of temperature was accompanied by a generalized itching, and the patient was covered with a papular rash for about 2 hours. Another attack of fever at noon on the 18th, and again for two hours, during the hot stage, the patient was covered with a diffuse urticarial rash with red, hot, vaso-paralytic intervening skin. Put on antimalaria treatment (a blood slide had shown young and adult schizonts and gametocytes of *Plasmodium vivax*). He had another mild attack of fever accompanied by an urticarial rash for 3 hours on 20th June. His examination showed a spleen just palpable and slightly tender, and marked tenderness in the McBurney area during the malarial paroxysm. Blood tests normal.

Having completed his antimalaria course, the patient was discharged on the 12th of June. Up to April 1945 he suffered no further relapses.

Case 2.—G. R., male, aged 28, admitted under my care on 13th July, 1943. Malaria (vivax) in 1942, relapsed in March 1943. On the 12th, a typical attack of malaria accompanied by severe generalized itching and, during the hot stage, by a papular rash which disappeared in few hours. A new paroxysm on 14th July, accompanied by an urticarial rash, lasted two hours during the hot stage. A blood slide showed trophozoites and gametocytes of *Plasmodium vivax*. The patient underwent a course of antimalaria treat-

ment and made an uneventful recovery.

Case 3.—G. C., male, aged 49. Admitted under my care on 18th September, 1943. Malaria (vivax) in 1940, relapsed in June 1941 and September 1942. On the 16th he had a typical attack of malaria accompanied by a very pruriginous, papular rash, lasting about 2 hours during the hot stage. He was admitted in the afternoon of the 18th during the hot stage of another paroxysm of malaria, covered with large elements of urticaria which lasted about 3 hours. He had taken no quinine. As his blood showed the presence of infestation with gametocytes of *Plasmodium vivax*, he underwent a regular antimalaria course and made an uneventful recovery.

There is almost complete agreement to-day in considering a great part of the clinical pictures and conditions which may occur during or may complicate a malarial attack as due to idiosyncrasy.

Asthmatic attacks (Thonnard-Neumann, 1928) during a malarial paroxysm, urticarial rashes (Eyer mann and Strauss, 1930; Davies, 1936; Gouriou, 1938; Chatterjee, 1939; Agrama, 1940) in patients who have taken no quinine or any other antimalaria drug, epileptic fits and symptoms of acute aseptic meningeal reaction (Davies, 1936), abortive attacks of acute appendicitis (Raven, 1944) and many other conditions are all interpreted as expressions of idiosyncrasy to different substances connected with the malaria infestation. Many symptoms of the malarial paroxysm itself are interpreted in the same way. So Abrami and Sevenet consider the hyperpyrexia of the malarial attack as expression of an anaphylactic or a hæmoclastic shock. Vasomotor troubles (vascular hypertonus during the stages of rigor and heat, hypotonus during the stage of defervescence) are also considered by Brown (quoted by Castellani and Chalmers, 1919) as the result of idiosyncrasy.

Either the shower of merozoites or the by-products of the destroyed erythrocytes or of the parasite (? hæmozoin) may act as foreign proteins when present in the blood stream, and may cause of the patient to them.

Summary

Three cases of urticaria occurring during a paroxysm of malaria are described on account of its rarity. The possible mechanism is discussed.

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A Mirror of Hospital Practice

MALARIA CONTRACTED AFTER SPLENECTOMY FOR SPLENOMEGALY PROBABLY CAUSED BY KALA-AZAR

By JOHN LOWE, M.D. (Birmingham)

THE case here briefly presented shows certain points of interest.

The patient was apparently well until 1944 when he had an attack of fever with splenic enlargement, which was at that time considered to be due to kala-azar, but for which the patient did not take treatment. Later in the year he was admitted to a Calcutta hospital where the diagnosis of tropical or Bengal splenomegaly was made and splenectomy was performed. At the time of splenectomy it is recorded that the liver was slightly enlarged. His recovery after operation is said to have been uneventful, but his stay in hospital was prolonged, possibly for the treatment of anaemia and other manifestations of kala-azar. He was discharged from the hospital in March 1945.

In April 1945, he had an attack of fever, and later he came back to the same hospital for diagnosis and treatment. The clinical picture suggested kala-azar and the complement-fixation test (with WKK antigen) was done by the Kala-azar Department of the School of Tropical Medicine with a positive result. There is however no record of sternum puncture or of the finding of *L. donovani*. The fever, however, responded to treatment for kala-azar. During this time also the liver was found to be enlarged.

In July 1945, the patient had another attack of fever with chill, rigor, headache, pain in the body, etc. When this fever had continued for two weeks he came to the School of Tropical Medicine. Blood examination revealed a moderately heavy infection with *P. vivax*. He was admitted to hospital, and on that day his temperature rose to 104.8°F. The spleen, having been excised, was not palpable, but on admission the liver was greatly enlarged and tender, reaching down to the level of the umbilicus.

The fever responded promptly to treatment with mepacrine, the temperature was controlled in three days and the blood also became negative in three days. During treatment, the size of the liver became less, and the patient was discharged from hospital a week after admission. A week later he came for examination and the size of the liver was still further reduced.

The following points are noted in this case : (1) The probability that in this case splenectomy was performed because the cause of the splenomegaly (namely kala-azar) was not detected. (2) The severity of *P. vivax* malaria after splenectomy. The fever continued for a

fortnight and at the end of this time was still high. In people living in endemic areas, with possibly some acquired immunity, untreated malaria does not usually last as long as this, and the temperature would normally have been lower at the end of two weeks. (3) The part played by the liver in malaria in the absence of the spleen.

While the liver was perhaps slightly enlarged before malaria, yet the malaria was accompanied by a very marked enlargement of the liver which apparently took on many of the functions normally performed by the spleen. The decrease in the size of the liver, when the malaria was controlled, was rapid and marked.

The findings in this case would indicate strongly : (i) That in areas where malaria and kala-azar are endemic, the spleen should not be removed without adequate steps to exclude kala-azar and malaria. (ii) Persons who have had their spleen removed should take steps to prevent getting malarial infection, and, if they do get infected, prompt diagnosis and thorough treatment is essential. Fortunately in this case the parasite was *P. vivax*; it is considered possible if not probable that an infection of *P. falciparum* in this patient would have proved fatal.

A CASE OF RIGIDITY OF CERVIX

By Dr. (Miss) JIWAN LATA, M.B., B.S.

Mrs. G. L. Maternity Hospital, New Delhi

THE patient was a well-built Hindu female, a primipara, aged 23 years, with quite a broad pelvis, and a full-term pregnancy. A month before delivery, she started getting oedema of the feet. Repeated examinations of the urine and blood pressure revealed no abnormality.

Pains started on the morning of 4th October, 1945. She was given an ounce of castor oil. The pains increased by the evening but there was no advance. The cervix dilated a little, admitting one finger. Morphine and atropine were given at about 2 a.m. that night. She slept for a few hours and when she woke up the pains increased. Two doses of quinine sulphate were given. In spite of frequent and strong pains, the cervix did not dilate, though it felt quite healthy. Several remedies were tried, e.g. morphine, atropine, chloral hydrate, potassium bromide and rectal douches but the cervix did not dilate. The urine showed much albumin; the blood pressure was systolic 122 mm., and diastolic 80 mm. Finally, after 36 hours of treatment, it was decided to deliver the patient by Caesarean section in spite of the fact that frequent pelvic examinations (five) had been done. A living male child was born. Soluseptasine was given as a prophylactic. The patient made an uneventful recovery. There was no apparent cause for the rigidity of the cervix and there was not a trace of sepsis in spite of the repeated pelvic examinations.

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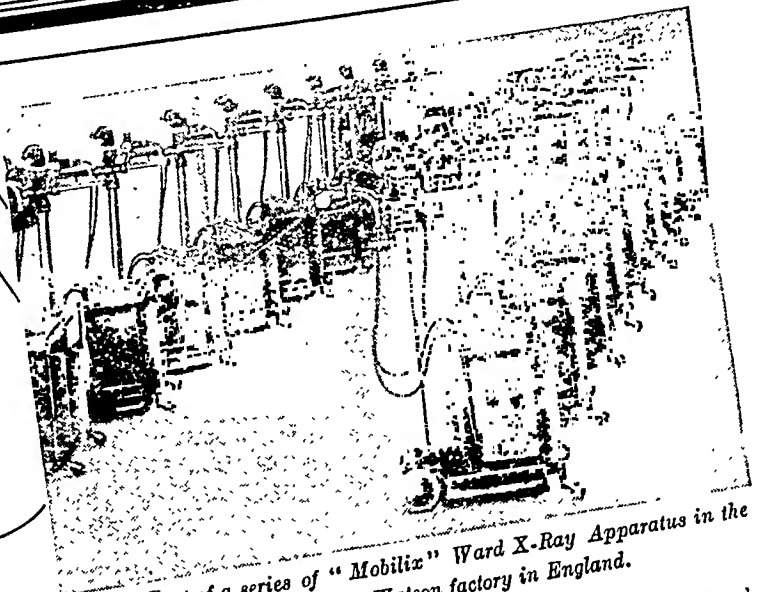
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Indian Medical Gazette

NOVEMBER

TREATMENT OF INDIAN KALA-AZAR

ON the whole, the treatment of Indian kala-azar is extremely satisfactory. The present position regarding treatment, with a variety of pentavalent antimonial preparations at our disposal, and with the aromatic diamidines, particularly stilbamidine, for the treatment of the few antimony-resistant cases, was discussed last year in an editorial (*Indian Medical Gazette*, LXXVIII, April 1943, page 201); the cure rate in Indian kala-azar is high. Moreover the deaths in kala-azar are due usually to secondary infection and complications, bronchopneumonia and, in children, cancrum oris with septic pneumonia being important causes of death. In the treatment of these complications, the sulphonamides and penicillin now play an important part. In cancrum oris in particular, penicillin applied locally and by intramuscular injections has vastly improved the prognosis.

There do remain, however, certain practical difficulties in the treatment of kala-azar on a large scale in endemic areas. Kala-azar is extremely common in young children; most of the pentavalent antimony compounds available have to be given by intravenous injection; these intravenous injections in young children with small veins, often collapsed, are not easy to give; in an outpatient department which may be attended by dozens or hundreds of such patients, the giving of these intravenous injections is a difficult task necessitating a highly skilled staff and much time. It is in this work that the need for an antimony preparation suitable for intramuscular administration is very greatly felt.

Before the war, the drug solustibosan (sodium antimony-v-gluconate) was introduced by the German workers, but the trials made in India with this drug in kala-azar gave results which on the whole were disappointing. Moreover, in those days there was available the German preparation neostibosan, which could be given intramuscularly if necessary, and which gave excellent results. During the war, neostibosan disappeared from the market, and no substitute for it has yet been produced. British and American firms, however, have marketed an equivalent of solustibosan, and in the last few years various workers in India have been studying further the action of this drug. In 1944 we published an article by Burke and Chakravarty reporting good results, and after reading this article we suggested further trials in the School of Tropical Medicine, Calcutta. The report on these trials is published

in our present number. In the meantime, however, Chakravarty has also carried out further studies and published in our last issue an article on the subject. Other workers have also been studying this matter in India and elsewhere. In India, Patel reported on this drug in 1944.

The position is now becoming clearer. Sodium antimony-v-gluconate is rapidly excreted in the urine. In order to secure an adequate therapeutic effect in kala-azar, it is necessary to give doses much larger than those originally used, which were calculated on the basis of the antimony content. It is now found that daily doses up to 20 c.cm., containing 20 mg. of metallic antimony per c.c., are needed in an adult, and are well tolerated, the dosage in children of course being smaller.

The size of this injection is a drawback, and more concentrated solutions of this drug have been prepared and used with apparently good effect, but in Calcutta at any rate this concentrated solution when injected intramuscularly has given rise to severe pain.

The work outlined above has been done mainly with stibatin (Glaxo). Certain Indian firms are now marketing similar preparations. One such Indian preparation recently tested in the Calcutta School of Tropical Medicine gave rise to severe pain and abscess formation at the site of injection in every case in which it was given. These difficulties should be overcome later.

It is still too early to express a sound opinion on the value of this drug in Indian kala-azar, because accurate figures for relapse rates after full doses are not yet available in a large series of cases; these are necessary for accurate assessment. It appears from results now becoming available that the relapse rate may be rather higher than is seen after the more usually used antimony preparations. Nevertheless it does appear that in this drug we have a valuable aid in the treatment of kala-azar, particularly in children in whom repeated intravenous injections, often given in an outpatient clinic, do present considerable difficulty.

J. L.

GENERAL MEDICAL PRACTICE

IN different countries and in different circumstances, conditions of general medical practice vary very greatly, and also standards of general medical practice vary. The general practitioner, as has often been said, is the backbone of the medical profession, and the maintenance of a really adequate standard in general practice is essential, if the profession is to secure and maintain the confidence of the public, and to make its contribution to the health and welfare of the country.

We think that there is general agreement that the general standard of general practice in India is not what it ought to be. There are numerous reasons for this, of which we can here

enumerate only a few. Sometimes the doctor's general and medical education and training have not been of sufficiently high standard to enable him to grasp fully and to practise good scientific medicine; even a good man with good training will find the practice of good scientific medicine frequently difficult or impossible. Careful and thorough clinical examination of the patient is often very difficult in the circumstances in which the doctor has to work. His financial resources are often very limited and his income very small. He has no properly equipped consulting room, and when he sees patients in their own homes, conditions are often even less favourable. He is unable to afford the equipment necessary for good practice, and his patients are often so few and so poor that they cannot possibly remunerate him for the type of service which scientific medicine demands. Good scientific medicine may not pay, whereas quackery often pays handsomely. It is only a doctor in a sound professional and economic position who can afford not to practise quackery, who can tell his patients that no medicine he can give is likely to be beneficial, or that treatment for the condition is likely to be long and difficult and results uncertain, or that treatment in hospital with adequate facilities is the only treatment which is likely to be a success. The temptations to quackery are great: most people in India does not understand scientific medicine, what it can do and what it cannot do, and they will flock to any quack who claims to cure any and every condition by some wonderful and usually useless remedy. Many people also have an extraordinary craving for injections, and think that doctors, unless constantly giving injections, are not doing their job properly. Many injections given in medical practice in India are unnecessary; for example the routine use of quinine injections in the treatment of malaria, the routine giving of intravenous glucose in any patient with fever, the vast number of calcium injections, and nowadays injections of vitamins. Most of these are unnecessary and their unnecessary use constitutes quackery.

The doctor in practice is often not in a position to refuse to do these things, and moreover in his poor financial position he cannot ignore the fact that his remuneration for injections is much higher than for ordinary prescription of medicine to be taken by the mouth, or for telling the patient the truth, such as that no medicine taken orally or by injection is likely to be of benefit. The Indian public has not yet realized that, when they go to a medical man, they go to him not necessarily for a prescription or for an injection, but for good examination and sound advice based on sound training and experience.

Thus we have in India the rather anomalous and rather tragic position of having far too small a number of doctors trained to practise scientific medicine, while at the same time most

of these doctors, in the circumstances in which they have to work, find themselves very often quite unable to practise sound scientific medicine.

How is this position to be remedied? It will obviously take a long time. The general standard of education, general and medical, of doctors must be improved. Their economic condition must also be greatly improved. The miserably low pay frequently given to qualified medical men must be greatly increased. A good doctor should be able to command reasonable fees from his patients who can afford to pay him, and, for those who cannot afford to pay fees, greatly increased provision for public medical services should be made. Doctors should be encouraged and enabled to practise medicine on sound lines, and to reduce and finally abolish the quackery which is so often seen now. This may not be possible until there is a great improvement in the economic and educational standards of the people, so that they will not only learn what scientific medicine can do, but will demand good scientific medicine for themselves, and, moreover, will be in a position to pay for it, either individually or collectively through publicly provided medical services. This is perhaps a dream of the future, but this is the goal towards which we must strive.

This problem is not peculiar to India, although in India it is seen in a very acute form at the present time. It is seen in all countries. In England the same problem is being encountered; attempts are being made to face it, and various plans and schemes have been made to improve the standard of medical service in general, particularly of general practice, and make medicine of a higher standard available to everyone. Nevertheless even to-day a good doctor can do excellent work in general practice. This is shown by a very interesting review of a year in general practice written by D. R. Snellgrove and published in the August 1945 number of *The Practitioner*. We think this review must be of interest to many practitioners in India, and we therefore abstract it here.

This doctor is one of four in partnership, with his own panel of 2,000 patients and about the same number of private patients. He has a surgery built for the purpose in the garden of his house, with a waiting room to seat 30 and a consulting room and a dispensary. His wife, a trained nurse, acts as nurse receptionist, does dressings, assists in dispensing, keeps the appointment book, gives some injections and helps in many ways. All the work of the practice is carefully recorded, and this review is based on the records of one year with 289 working days and, in all, 708 'surgeries.' Fourteen thousand and five-hundred patients visited the surgery, and nearly 4,000 patients were visited in their homes. Eleven thousand prescriptions and 9,000 certificates were given.

About 3,000 medicines were dispensed. The daily average number of patients for 310 days was 60. The following table gives the work done in addition to ordinary clinical examination :—

Anæsthetics	87
Antenatal examinations	52
Aspiration (bursa)	12
(ganglion)	5
Coagulation time	6
Dilatation of prepuce	32
Dressings	518
Ears syringed	120
Foreign bodies removed from eye	41
Full blood counts	28
Hæmoglobin estimation-	41
Injections	812
Microscopical examinations	91
Minor operations	28
Number of births	9
Paracenteses	21
Patch tests (for tuberculosis)	8
Pathological specimens sent	30
Pessaries fitted (watch spring)	6
Repair of perineum (midwife's calls)	8
Sedimentation rate estimations	56
Skin tests	13
Sutures inserted	32
Sutures removed	71
Transfusions	3
Urine analyses	297
Vaccinations	5
Varicose veins injected	58

Regarding the above table the author writes as follows :—

'The table collects together some of the various activities of general practice. It is interesting to consider and explain a few of these. One of the transfusions was plasma, given for post-partum hæmorrhage and shock, to a patient who also had inversion of the uterus (she did well) ; another was for a dehydrated patient in a caravan. Some of the microscopical examinations consisted of blood films for differential counts, centrifuged urine deposits, skin sections, sputum, vaginal smears, faeces, hairs (for tinea) and the hunt for scabies. The sedimentation rate was estimated as a routine for tuberculous and rheumatic patients and in some obscure cases. The practice is in an industrial district, and foreign bodies in the eyes are common. Skin tests were used for asthma, allergy and for a few dermatological conditions. A patient with inoperable carcinoma of the ovaries and extensive secondaries, and a young girl with mitral valve trouble and congestive heart failure were tapped frequently. Minor operations consisted of removal of sebaceous and Meibomian cysts, moles, plantar warts, toe nails ; myringotomy ; thrombosed piles ; circumcisions ; and opening of abscesses. All dressings that can possibly be done there are dealt with at the surgery. Injections include those for varicose veins, pernicious anæmia, whooping cough and diphtheria (passive and active immunization), tetanus (prophylaxis) and a large number, using procaine, for some rheumatic conditions, e.g. lumbago, fibrositis, sciatica, and for fractured

ribs and sprains. Hæmoglobin estimates were made routinely in all pregnant women (Gower's method). The 87 anæsthetics include dental gases, ethyl chloride, sodium pentothal and open ether. Only 8 patch tests were done for tuberculosis. The number of ears syringed 120, seems large, but this was never done unless on auriscope examination it was found to be necessary, and in each case the wax was "softened" for at least two days with sodium bicarbonate ear drops. The nine births include one set of twins.'

The review then deals with different groups of diseases seen. One hundred and forty-three cases are classed as infective diseases, included one case of leprosy contracted in Africa, cases of chicken pox and mumps, pulmonary tuberculosis, syphilis, scarlet fever, gonorrhœa, whooping cough, measles, meningitis, pneumonia, malaria and vulvo-vaginitis. Four hundred and fifteen cases are classified as skin diseases. Many cases of industrial dermatitis were seen. Other cases included *T. cruris* infection and epithelioma of the skin ; contact dermatitis, one due to spectacles and another due to antiseptics, and several caused by hair dyes and cosmetics, two caused by metal suspender parts, one by earphones, two by soap ; septic fingers, impetigo contagiosa, scabies, eczema, acne, lupus vulgaris, varicose ulcers, and numerous other skin conditions are recorded.

Three hundred and ten cases are classified under diseases of ear, nose and throat, and details are given. Diseases of women numbered 222 cases, including 30 abortions, and details of these are given. Metabolic and deficiency diseases encountered included ariboflavinosis, diabetes, and obesity. Diseases of the bone and muscles numbered 337, including one case of osteomalacia, 34 fractures including a spontaneous fracture caused by sarcoma, and 170 cases of rheumatism are included. Lumbago, fibrositis and sprains and allied conditions were treated with local injections of procaine with excellent results. The diseases in this group included sprains, claw foot, Dupuytren's contracture, internal derangement of the knee, flat foot, trigger finger, and many others.

Diseases of the digestive tract numbered 285, and included one case of intestinal obstruction due to strangulated hernia ; peptic ulcer, dyspepsia and gastritis were common. Two cases of perforation were recorded, and 8 cases of appendicitis, 5 being operated on. One case of congenital pyloric stenosis was seen. Cholecystitis, colitis and roundworm infection were encountered. The treatment for threadworm is discussed. Three hundred and one cases are recorded under diseases of the respiratory tract including influenza, common cold, catarrh, asthma, pulmonary tuberculosis, pneumonia, bronchitis, etc. Diseases of the blood included 271 cases, one case of hæmophilia, 22 of hypertension, and cases of pernicious anæmia, con-

gestive heart failure, coronary thrombosis, varicose veins, agranulocytosis, angina pectoris, bacterial endocarditis, cerebral hæmorrhage, valvular disease of the heart and numerous others are mentioned. Diseases of the nervous system recorded a total of 180. Most numerous was 'neurasthenia'. Cases recorded included amyotrophic lateral sclerosis, disseminated sclerosis, epilepsy, paralysis agitans, Raynaud's disease and others. Diseases of the genito-urinary system numbered 101, including cases of polycystic kidney, bacilluria, cystitis, renal calculus, nephritis, pyelitis, enlarged prostate and carcinoma of the prostate. Eye diseases numbered 155, including conjunctivitis, errors of refraction, various inflammatory conditions, cataract, herpes ophthalmicus, trachoma and others.

This is a very brief summary of the analysis of one year's work of the general practitioner, all the work being carefully recorded. When we consider this review, we are struck by certain things; by the great amount of work, by the great variety and range of the work, and the vast knowledge of medicine which may be necessary to deal with it. General practice of this kind needs highly skilled personnel, not only for the clinical work but for the other work involved. It is striking that a very busy practitioner himself does a considerable volume of laboratory work including blood counts, hæmoglobin estimations, sedimentation rate estimations, urine analysis, etc. We wonder how many general practitioners in India are equipped to carry out such a range of activities as is here recorded, how many even have a microscope and use it regularly, as apparently this general practitioner does. Here in India with malaria and dysentery so common in which microscopical examination is of great value, not many general practitioners own a microscope, and fewer still use it.

We think that many practitioners in India will be interested in this account of a year's general practice and the great variety of activity which it includes. We doubt if this account is typical of general practice in England as a whole; in fact, we are fairly sure it is not; but it will be even less true of general practice in India. All practising physicians can learn much from such accounts of general practice; we must work for the day when the whole standard of general practice everywhere will be raised; when all doctors will have the necessary knowledge, equipment and financial resources, and when the conditions of their work will be such as to enable them to attain the highest possible standards.

J. L.

LIMITATIONS OF SULPHONAMIDE THERAPY IN SURGERY

In the treatment of wounds, the local application of sulphonamides has often failed

because their action is apt to be neutralized by chemicals, pus and dead bacterial cells. This matter is discussed in a report recently issued by a special Medical Research Committee*. The results are based on records of 926 soft-part wounds, 674 compound fractures and 591 burns, the groups being divided in basis of certain common factors. Of the soft wounds treated with sulphonamides, either systemically alone, or locally alone, or both, infection occurred in 20.4 per cent compared with 12.4 per cent in the group treated with no sulphonamide. It will come as a shock to many surgeons that a higher percentage of infection followed its use in the peritoneal cavity. More or less similar results were obtained also in compound fractures and burns in which the evidence indicated that its local use as a prophylactic agent was of no value, but it is useful in treating cases of infection by reducing the spread from the original site.

This report indicates that while the systemic administration of sulphonamides is efficacious in limiting the spread of infection and preventing septicæmia, the routine local use of these drugs in the early stages for prophylactic purposes is practically futile, and that, if this is omitted, a great waste of material is avoided and many toxic reactions prevented.

These findings are rather at variance with findings reported by others, but they do give a timely warning of the marked limitations of the local application of sulphonamides.

R. N. C.

Special Article

SOME ASPECTS OF MALARIA THERAPY ON THE EASTERN FRONTIER OF INDIA 1942-44

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Introduction

An attempt is made here to give a short account of the problems of malaria therapy experienced in the eastern frontier part of India during the above period and of the measures taken to deal with them under the direction of the Headquarters, India Command.

After the Japanese army occupied Burma they halted on the Indo-Burma frontier. In this intensely

* Meleney, Frank. L. *Surg. Gynec. and Obst.* 80, 263. (1945.)

malarious area a containing force was maintained to oppose any attempt at Japanese invasion of India. Malaria was exceedingly common, and the official figure for 1942 was 76,000 cases, certainly an under-estimate, since many cases were treated in their own units owing to lack of accommodation and were thus not recorded. The medical services of India were greatly strained by the loss of medical units in Malaya and Burma and by the absence of others serving in the Middle East. The number of hospitals and smaller units was grossly inadequate. Many of the medical units in the field had recently been raised, and were short of staff and particularly of trained personnel. Lines of communication were long and, during the monsoon, roads were often washed away. Evacuation of casualties was difficult and delayed. The supply of drugs from overseas was uncertain and intermittent. While collecting data on the conditions under which malaria was being treated in the field, the writers found that evasion of treatment was frequently successful, that medical units were understaffed to such an extent as to make it exceedingly difficult for them to ensure that all medicines prescribed were swallowed, and that the high black market prices for drugs provided a strong incentive for theft. This was the situation confronting the physicians of the Eastern Army in 1942.

The year 1943 was characterized by inconclusive fighting and incessant patrol activity along the frontier, and the malaria casualties reported for 1943 were more than double those of 1942, but in 1943 many more troops were involved and malaria statistics were much more accurate. It is very doubtful if there was any real increase in the incidence of malaria in this year. A considerable number of cases with symptoms of pernicious malaria was reported. In one hospital alone, 54 cases of malarial coma were admitted during six months. Nevertheless, the number of such cases was not disproportionately high in relation to the total of malaria casualties.

The spring of 1944 saw a determined Japanese attack against India. The Japanese army was, however, defeated and driven back by the 14th army. In this achievement the medical services contributed greatly. The mortality rate from malaria for the epidemic months of June and July was 0.5 per cent, and this in spite of the fact that the nature of jungle warfare caused many cases of malaria to be admitted to hospital in an advanced stage of illness and also suffering from exhaustion and exposure.

Therapeutic trial of the standard army treatment and its modifications

The Director of Medical Services in India instituted an investigation into the effect of standard treatment in the field, and the authors

troops for five days. This treatment had given satisfactory results in peace time, but before long doubts were expressed as to its efficacy under war conditions. The main defects ascribed to it were failure to control pyrexia and parasitaemia, and inability to prevent relapses. Some critics stated that the British and American brands of mepacrine and pamaquin were inferior to their German prototypes. Opinions were also expressed that the clinical forms of malaria in Assam were severe and resistant to orthodox methods of treatment.

The following is a brief outline of a therapeutic trial carried out from December 1942 to February 1943 in an Indian General Hospital at Dimapur, a village in the jungle of a highly malarious area.

Treatments used

- A. Standard treatment (army in India).
- B. Standard treatment using Bayer's atabrin and plasmoquine in place of mepacrine and pamaquin.
- C. Standard treatment modified by prolonging the quinine period until fever had subsided.
- D. Standard treatment modified by commencing with mepacrine and giving quinine grains 20 daily throughout the ten days of mepacrine and pamaquin administration.

In all instances, drugs were given by the investigating medical officers who ensured that they were swallowed.

Series of cases

Cases with positive blood slides were selected freely for trial; the only grounds for rejection being intercurrent illness or pernicious symptoms requiring intravenous therapy.

Treatments A, B, C and D were given in rotation until two hundred and sixty cases had been admitted. Thereafter cases were allotted to treatments by species diagnosis in order to achieve a constant species ratio in each treatment group. This ratio which was determined by the relative incidence of the different species of infection may be tabulated thus:—

TABLE I

Species	Indian			British			Total cases in each treatment group
	B.T.	M.T.	Mixed (including quartan)	B.T.	M.T.	Mixed (including quartan)	
	34	26	15	9	6	2	92

with a small technical staff were sent to Assam for this purpose.

At this time the standard army treatment for malaria in India consisted of quinine grains 30 daily for two days, mepacrine 0.3 gramme daily for five days, a 'rest' period of two days, and pamaquin 0.02 gramme daily for Indian troops and 0.03 gramme daily for British

The ratio of first attacks to relapses and re-infections among British troops, who gave a reliable history, was 1:3.

The small series of British cases was treated to ascertain if their relative absence of immunity made them resistant to treatment. All cases were observed for one month after treatment was commenced.

Results

The more important results are given in table II :—

TABLE II

Treatment	Average period in days required to		Average reduction in spleen during treatment in finger-breadths	Relapses during observation
	control fever	terminate parasitæmia		
A	2.0	2.7	1.7	2 or 2.2%
B	1.5	2.7	1.9	6 or 6.5%
C	1.6	2.8	1.8	7 or 7.6%
D	1.7	3.0	1.7	4 or 4.3%
All treatments (368 cases).	1.7	2.8	1.8	19 or 5.2%

Conclusions

It was clearly demonstrated that the standard treatment was effective for the treatment of the acute stage of uncomplicated cases of malaria occurring under war conditions in Assam. No evidence whatsoever was found to suggest that the type of malaria encountered in Assam was resistant to treatment. There was no appreciable difference between British and Indian troops in the response to treatment, nor between the effect of the synthetic drugs of Bayer and that of those of British origin. Results obtained with an increased dosage of quinine in treatments C and D were not appreciably better than those obtained with standard treatment. The early relapse rate was moderately high; there were three relapses during treatment, all falciparum, and sixteen after treatment, ten vivax and six falciparum. This was not unexpected in view of the fact that the majority of cases treated had almost certainly been repeatedly infected in spite of the rigid anti-malaria discipline enforced. The number of cases in each treatment group was too small to warrant analysis of the effect of each treatment upon the infecting species.

Trial of a shorter treatment than the standard treatment

In 1943, more medical units were available to deal with malaria, and also a new type of unit, the Malaria Forward Treatment Unit, was evolved to meet the situation. These units are in effect small general hospitals simplified and adapted for malaria diagnosis and treatment. Special care was given to seeing that the standard treatment was properly taken and not evaded. Two stubborn clinical problems however persisted. The first was the length of time spent off duty by troops undergoing treatment for malaria in hospitals, and the second was the persistently high relapse rate of the benign tertian malaria.

Attempts were made to find out whether a shorter treatment could be effectively employed. Thirty grains of quinine daily for 7 days and pamaquin 0.02 gramme daily from the 3rd to the 7th day was one treatment tried. The ratio of falciparum to vivax infections was 2 to 1, and there was a small number of mixed infections. The treatment was followed by a week's convalescence. At the end of this period one-third of the cases was fit for combatant duty, one-third fit for ordinary duty, and one-third required further treatment of convalescence. Owing to quinine shortage, this treatment could not be continued. The main lesson of this trial was that a fresh attack of malaria is a debilitating illness requiring at least 2 or 3 weeks for full recovery.

Regarding the problem of relapse it was realized that the relapse rate was intimately related to the number of infections acquired by the individual concerned. This fact however did not help directly in the solution of this problem.

Trial of treatments embodying a heavy initial dose of mepacrine

At this time, the researches of Shannon and his collaborators in America into the pharmacology of mepacrine became known in India. They showed that the blood mepacrine levels showed a cumulative rise throughout the ordinary therapeutic course, owing to the slow degradation and excretion of the drug by the body. These facts revealed an important weakness of the standard treatment, that it failed to establish a consistent level of schizonticide in the blood for some time after the quinine administration ceased. Shannon suggested that a rational mepacrine treatment should begin with a high dose of mepacrine, and this marked a notable advance in the therapeutics of malaria, and had an application in the problem of relapsing benign tertian malaria. It was decided in India to carry out field therapeutic trials based on Shannon's work.

An extensive malaria therapeutic trial to evaluate treatments embodying an initial heavy dosage of mepacrine had been planned early in 1944, but before this plan was put into effect, certain proposals by the Medical Research Council on the subject came to hand, and these were incorporated in the plan for the forthcoming therapeutic trial. The trial was carried out in Assam in medical units of the 14th army. It was directed by one of us (J. M. R.) and the other (A. E. R. C.) was in charge of the pathological work.

The general plan of the trial

The general plan of the trial conformed as closely as was practicable to the memorandum issued by the Medical Research Council, with minor modifications necessitated by practical considerations.

Treatment.—The following courses of treatment were used:—

Course A, army standard treatment

Quinine 10 grains 3 times daily in solution for 3 days.

Mepacrine 0.1 gm. 3 times daily for 6 days.

Interval for 2 days.

Pamaquin 0.01 gm. 3 times daily for 3 days.

Total duration, 13 days—quinine 90 grains.

mepacrine 1.5 gm.

pamaquin 0.09 gm.

Course B, mepacrine, initial high dose and short duration

Mepacrine 0.2 gm. every 6 hours for 48 hours.

Then 0.1 gm. 3 times daily for 5 days.

Total duration, 7 days—mepacrine 3.1 gm.

Course C, mepacrine, medium-sized initial dose and short duration

Mepacrine 0.2 gm. 3 times daily for 1 day.

Then 0.1 gm. 3 times daily for 6 days.

Total duration, 7 days—mepacrine 2.4 gm.

Course D, mepacrine (like C), plus pamaquin

Mepacrine 0.2 gm. 3 times daily for 1 day.

Mepacrine 0.1 gm. 3 times daily for 6 days.

Pamaquin 0.01 gm. 3 times daily for 3 days.

No interval between mepacrine and pamaquin.

Total duration, 10 days—mepacrine 2.4 gm.

pamaquin 0.09 gm.

(Alkali was given during the mepacrine course in order to render the urine alkaline before pamaquin was due.)

Course E, mepacrine, initial dose of 0.8 gm.

Mepacrine 0.8 gm. *stat.*

Mepacrine 0.1 gm. 3 times daily thereafter for 7 days.

Total duration, 7 days—mepacrine 2.8 gm.

Experimental subjects.—As so many variable factors enter into the aetiology and progress of an individual case of malaria, it was decided that a minimum of two hundred cases should be treated with each treatment. It was considered unlikely that sufficient British troops suffering from malaria could be concentrated in any one centre during a period suitable for the trial to allow of fulfilment of this criterion. At the time when the trial was carried out, operational conditions in Assam were such as to make it impossible for research work to be divided up between various centres. Accordingly after careful consideration, it was decided to restrict the trial to one centre and to carry it out exclusively on Indian cases.

Site of the trial.—An Indian General Hospital, situated on the Brahmaputra river at Gauhati in Assam, was selected as the site for the trial. Special wards of the hospital were devoted exclusively to the trial. Gauhati is some one hundred and seventy miles from the Burma border and is surrounded by areas where

malaria is hyperendemic, although the town itself is virtually free of malaria. An earlier attempt to carry out a therapeutic trial at Dimapur, which is considerably nearer to the border, was frustrated by the Japanese advance into Manipur State.

Season for the trial.—The trial was commenced in May and completed in September 1944. This period coincided with the epidemic months of the malaria season, thus ensuring an ample supply of malaria cases. It is reasonable to assume that the majority of these had been freshly infected. During the early stages of the trial there was a preponderance of malignant tertian malaria. Later malignant and benign tertian infections showed an approximately equal incidence. Throughout the trial, climatic conditions were characterized by considerable heat and extreme humidity.

Surveillance period after treatment.—After the completion of treatment, patients were sent for one month's surveillance to an Indian convalescent depot in Shillong which is situated at 4,500 feet above sea-level in an area free from malaria. This observation period was regrettably brief, but was dictated by operational considerations. Patients relapsing in Shillong or developing illnesses other than malaria were admitted to the Indian Military Hospital there which is also situated in a malaria-free zone. As the route from Gauhati to Shillong is malarious in certain parts, the trip between these places was carried out during daylight.

Detailed plan of the trial

Selection of cases.—Cases were selected from the casualty department of the hospital. The criteria of selection were as follows:—

(a) Cases had positive blood slides.

(b) They were free from complicating disease so far as could be ascertained by thorough clinical examination.

(c) They were not so ill as to require intravenous therapy.

(d) They had not received suppressive mepacrine within three weeks prior to admission. It will be apparent that cases with varying amounts of mepacrine in the blood are unsuitable for a therapeutic test.

Serial numbers and treatments were allotted to patients by rotation, without consideration of species diagnosis, thus: A1, B2, C3, D4, E5, A6, etc. Cases from 960 to 1,000 however were allotted treatments by species diagnosis in order to achieve a constant falciparum: vivax: mixed infection ratio.

Drugs employed.—(a) Quinine. This came from Java. Quinine mixture was regularly analysed and found satisfactory. (b) The mepacrine used was British and American. Samples were tested for solubility and found satisfactory. One hundred and twenty-one stool examinations carried out failed to reveal undissolved tablets. (c) The pamaquin used was

manufactured by Imperial Chemical Pharmaceuticals.

Drugs were given to the patients by two nursing sisters who witnessed the swallowing of the drug by the patients and inspected the mouths afterwards. Drugs were as far as possible given after food. Vomiting of drugs presented a difficult problem. Instructions were issued that where quinine was vomited within half an hour of administration the dose should be repeated. With mepacrine, tablets vomited prior to disintegration were repeated. If they had disintegrated and the vomit was coloured by mepacrine, one tablet was repeated if the vomit occurred within one hour of the dose being given. No restriction was placed on the use of diaphoretic mixtures, A.P.C. powders, etc.

Observations.—During the treatment the following observations were made:—

Temperatures were taken morning and evening, all readings being made after a full minute. The accuracy of the thermometers was tested. It was found that, under the climatic conditions prevailing, a considerable proportion of patients showed an evening temperature of 99°, and the same was found in the healthy staff. The interpretation of this rise of 99° therefore created some difficulty in establishing the termination of the malarial fever. A temperature of 99° following initial-pyrexia or coinciding with the rhythm of malarial fever was attributed to malaria.

The spleen was examined at the beginning and at the end of treatment, and in treatments A and D on the 7th day.

all thick films being examined by the pathologist. Crescent counts were carried out by the pathologist on the day when the treatment was completed. During the observation period, a thick drop film was examined three times during the first week, and once weekly during the 2nd, 3rd and 4th weeks. In this way, several parasite relapses were detected. Blood counts and hæmoglobin estimations were carried out at the beginning of treatment, at the end of treatment, and at the end of observation. Leucocyte counts were carried out at the beginning and end of treatment.

Observations were made on the possible relationship of mepacrine dosage to the changes in the differential count. Urine examinations were carried out for albumin and for the presence of quinine after 30 grains of quinine had been given. Studies were made on the relationship between mepacrine dosage and albuminuria, and of the urine of patients receiving pamaquin.

In a certain proportion of cases, intercurrent illness supervened during the course of treatment and observation. The most common were dysentery and short fevers of the dengue-sandfly group. Symptoms sometimes included severe headache, backache, and malaise. It was often thought that some of the symptoms might be manifestations of mepacrine toxicity, but this was later considered unlikely. Cases developing severe constitutional disease during treatment for malaria were discarded from the trial, and were replaced, but cases with minor ailments were retained.

TABLE III
Toxic reactions; number of cases affected

Species	Reactions	TREATMENT				
		(QM A period)	B	C	(M period) D	E
B.T.	Vomiting	12	13	10	10	24
	Diarrhoea	7	1	3	2	2
	Abdominal pain	1	1	0	2	3
M.T.	Vomiting	35	36	15	22	48
	Diarrhoea	6	0	2	7	6
	Abdominal pain	3	2	0	1	3
Mixed	Vomiting	3	4	3	2	5
	Diarrhoea	1	0	2	0	1
	Abdominal pain	0	0	0	0	0
Total irrespective of species.	Vomiting	50	53	28	34	77
	Diarrhoea	14	1	7	9	9
	Abdominal pain	4	3	0	3	6

QM = quinine-mepacrine.
M = mepacrine.

Blood films were taken twice daily from every patient immediately after admission, species diagnosis and rough parasite counts were made by the pathologist on thin films evenly spread. Thereafter thick films were taken twice daily,

Cases developing fever during the one-month observation at Shillong had blood films made and sent to the pathologist for confirmation.

Toxic reactions.—In order to simplify description, this section omits abnormal mental

states which are dealt with in the ensuing section. The toxic reactions reported in table III include vomiting, diarrhoea and abdominal pain. Headache has been omitted as it is impossible to differentiate between headache due to malaria and headache as a symptom of a toxic reaction during the acute stage of malaria. Complaints of headache *per se* were very uncommon after the acute stage had passed. Toxic reactions with pamaquin were negligible.

The following comments are made on the data in table III.

The incidence of vomiting is far greater in the E treatment group (starting with 8 tablets of mepacrine in one dose) than in the others.

materially less common with a light initial mepacrine dosage. Any attempt to attain a high concentration of mepacrine in the body during the early hours of treatment by giving a large initial dose of the drug orally is likely to be attended with an incidence of vomiting disproportionate to any advantage gained by this method of treatment.

Much of the diarrhoea observed was probably due to mild attacks of infective enteritis rather than to the drugs employed in the treatment.

Abnormal mental states.—All cases showing any mental abnormality are described in table IV which includes cases later discarded from the trial owing to the development of intercurrent disease.

TABLE IV
Abnormal mental states

Serial number	Species	Dose of mepacrine before onset, grammes	Treatment	Clinical detail
1	M.T.	Nil	A	Severe dysarthria, accompanied by moderate excitement at onset. Gradual complete recovery over 4 days.
2	M.T.	Nil	A	Transient period of excitement. Rapid recovery.
3	M.T.	Nil	A	Mild hysteria. Transient bizarre behaviour, e.g. washing himself in ward instead of ablution room.
4	M.T.	Nil	A	Hysterical hyperpnoea and excitement. Brief duration.
5	B.T.	Nil	A	Dull and apathetic. Psychiatric opinion, 'low grade schizophrenic'.
6	M.T.	1.6	B	Hysterical convulsions. Gross unsystematized movements. Immediate cessation after firm treatment.
7	M.T.	0.8	B	No previous history of fits.
8	M.T.	3.1, 5 days' interval. 1.3	B	Mild confusion and slow cerebration. Transient.
9	B.T.	1.9	B	M.T. rings relapse shortly after completion of treatment during detention with mild bronchitis. Relapse treated with a treatment. On 5th day of mepacrine became excitable, completely disorientated, refractory and partially collapsed after violent fit of coughing. Episode lasted about 30 minutes. Treated with sedatives. Recovery complete in 2 hours.
10	B.T.	0.6	C	Reliable stable patient with good record.
11	M.T.	0.6	D	Mental dulling, transient.
12	M.T.	0.6	D	Transient episode of excitement.
13	M.T. B.T.	1.3	D	Refractory, unco-operative, deliberately spitting out medicines. Discarded from trial. Recovery on tube feeding.
14	M.T.	0.7	D	Apprehensive and excitable. Transient.
15	M.T.	0.8	E	Hysterical analgesia—2 hours' duration.
16	B.T.	1.0	E	Hysterical convulsions. Tossing legs in air alternately. Rapid recovery with firm treatment. Previous history 3 similar attacks.
17	M.T.	1.0	E	Excitable, unco-operative. Refusing drugs and fluids. Discarded from trial. Satisfactory recovery.
				Mental dulling, transient.
				Suddenly became very excited. Demanded rice which he ate avidly. Drank 2 pints of water in a few gulps, belched and fell asleep. No further symptoms.

Among the other treatment groups, it is least common among C and D treatment groups, and approximately equal among A and B treatment groups. It is considerably greater in the falciparum series of cases than in the vivax series. It would appear that the incidence of vomiting is likely to be approximately equal between a quinine treatment and a mepacrine treatment starting with 0.8 gramme daily in divided doses of 0.2 gramme and that vomiting is likely to be

The following points relating to table IV are worthy of consideration:—

1. Thirteen cases in the M.T. and mixed series showed abnormal mental symptoms whereas only four cases in the B.T. series showed any mental abnormality. In view of the fact that cerebral malaria was common in Gauhati at the time when the trial was conducted, it is reasonable to assume that a considerable proportion of the mental abnorm-

alities noted in the M.T. series were the direct result of malaria. This assumption is strengthened by the fairly even distribution of mentally abnormal cases among the five treatment groups.

2. Mepacrine administration was continued in all cases after the onset of symptoms without further incident except in case 8 when it was stopped after the episode recorded.

3. The hysterical incidents recorded are not uncommon in the course of any moderately severe illness among certain of the races included in the trial.

4. The clinician (J. M. R.) in charge of the cases is of the opinion that in only two of the cases recorded above, viz, 8 and 17, could the abnormal mental symptoms be reasonably attributed to the effect of mepacrine.

Intercurrent illness.—Forty cases suffered from intercurrent illness during the trial and

were discarded. The most common illness was bacillary dysentery. Fifty-two cases developed mild intercurrent illness during treatment, but were not discarded from the treatment. Seventy-four cases developed intercurrent illness during observation.

Relapses.—As the treatments were of unequal length, only those relapses are reported which occurred during the first seven days of treatment (the duration of treatments B, C and E was seven days) in order to secure a basis for comparison. During the period of a treatment not included in the foregoing tables five relapses occurred and three relapses occurred during the corresponding period of D treatment. Relapses during the first 7 days of each treatment are recorded in table V, and relapses during one month after the completion of treatment are recorded in table VI. The criterion of a parasitic relapse was the return

TABLE V
Relapses occurring during first seven days of each treatment

Treatment	A			B			C			D			E		
	P.S.	P.	T.	P.S.	P.	T.	P.S.	P.	T.	P.S.	P.	T.	P.S.	P.	T.
<i>B.T. infections—</i>															
Homologous ..	0	2	2	0	1	1	0	0	0	0	0	0	0	2	2
Heterologous ..	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
<i>M.T. infections—</i>															
Homologous ..	1	0	1	0	0	0	1	0	1	0	0	0	0	3	3
Heterologous ..	1	1	2	1	0	1	1	0	1	0	1	1	0	0	0
Mixed infections	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
GRAND TOTAL ..	2	3	5	1	1	2	2	0	2	0	1	1	0	5	5

TABLE VI
Relapses occurring during one month after completion of treatment

Treatment	A			B			C			D			E		
	P.S.	P.	T.	P.S.	P.	T.	P.S.	P.	T.	P.S.	P.	T.	P.S.	P.	T.
<i>B.T. infections—</i>															
Homologous ..	9	1*	10	1	0	1	6	0	6	1	0	1	4	0	4
Heterologous ..	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
<i>M.T. infections—</i>															
Homologous ..	1	0	1	0	0	0	2	1	3	2	0	2	0	0	0
Heterologous ..	6	0	6	1	0	1	5	0	5	3	0	3	4	0	4
Total M.T. infection.	7	0	7	1	0	1	7	1	8	5	0	5	4	0	4
<i>Mixed infections—</i>															
Relapsed as B.T.	3	0	3	0	1	1	0	0	0	0	0	0	0	0	0
Relapsed as M.T.	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0
Total mixed infections.	4	0	4	0	1	1	0	0	0	0	0	0	0	0	0
GRAND TOTAL ..	31	1	32	3	2	5	20	2	22	11	0	11	12	0	12

* This case relapsed during the first seven days of treatment and is thus also included in table V.

P.S. = parasitaemia with symptoms.
P. = parasitaemia without symptoms.
T. = total.

of parasites in thick blood films after a clear period of forty-eight hours.

These figures show considerable differences in the relapse rate during the period under observation of the five treatment groups. These differences were maintained throughout the trial. The high incidence of heterologous relapses in falciparum malaria is striking, which indicates that many cases recorded as falciparum malaria were harbouring latent vivax infections. The following are the conclusions regarding relapses:

(i) Few relapses occurred during the first seven days of treatment, and the difference in incidence in the different treatment groups is not regarded as significant.

(ii) The relapse rate of falciparum malaria during the observation period was persistently low.

(iii) The over-all relapse rate for vivax malaria was considerable, and there was marked difference according to the treatment employed.

(iv) There is a marked relationship between the relapse rate and the total dosage of mepacrine employed.

(v) Treatment A (the standard treatment) is the least effective of the five treatments in preventing early relapse although it includes pamaquin. Any action of pamaquin in preventing relapses must be dependent upon the previous maintenance of a sustained effective therapeutic level of a schizonticidal drug in the blood for a reasonable period. Studies of blood mepacrine levels have shown that this is not achieved effectively in the early stages of the standard treatment. Among the three treatments employing mepacrine only, the relapse rate has shown an inverse relationship to the dosage of mepacrine. The relapse rate in the D treatment group over the C treatment appears to have been materially reduced by the administration of pamaquin.

(vi) It is possible that the treatment employing the heavier mepacrine dosage may have postponed relapse beyond the observation period. The follow-up period is too short to confirm or refute this possibility, but from a military point of view it is cogent to observe that the postponement of relapse is a desirable feature in a treatment which cannot claim to cure.

Sundry observations

Regarding the composition of groups under different treatments, the following remarks are made. As variations in racial immunity might be expected to effect the clinical response to malaria, steps were taken to see whether the distribution of different racial groups under the different treatments had been reasonably uniform. Similar steps were taken to see whether the composition of the five different treatment groups had been roughly the same from the point of view of possible acquired immunity. Accurate estimations are difficult to

obtain. The patients were classified into three groups: those who never had any malaria, those who had never had malaria in Assam although they had malaria elsewhere, and those who had had malaria in Assam previously, and the five different treatments were studied from this point of view. The five treatment groups were also studied with regard to the duration of symptoms before admission, and no major differences were found. Studies of body weight in the five different groups also showed no major difference, as also studies of the parasite counts made in the different groups. All these observations tended to indicate that the five treatment groups were comparable and that there was no factor operating in any one group which would influence the results of the clinical test.

Studies were made of the crescent counts in the five treatment groups, the observations numbering 6,000. The findings were as follows: No crescents were found during the observation period among cases receiving treatments A and D which include pamaquin. Among treatment groups B, C and E the number of crescents detected during the observation period bore a close relation to the total dosage of mepacrine. This relationship was absent during the first week of treatment.

Studies of blood counts and hæmoglobin estimations in cases of *P. vivax* and *P. falciparum* malaria under the five different treatments were made, and the following conclusions were arrived at:—

1. There is no significant difference between the five treatment groups in the rate or degree of blood destruction and regeneration.

2. The initial erythrocyte level in the vivax series is considerably below that of the falciparum series, whereas the difference in the hæmoglobin levels is slight.

3. The most important hæmatological finding from the operational point of view is the establishment of the fact that irrespective of the treatment used, approximately ten and thirty days were required to restore the erythrocyte count in the vivax series to the original level and to five million red cells respectively. In the falciparum series the corresponding periods were twenty-five and forty days. It is possible of course that the rates of regeneration might have been accelerated to some extent by iron therapy.

Leucocyte counts in vivax and falciparum malaria under different treatments were also studied. A moderate rise in the leucocyte count at the end of treatment was demonstrated in all treatment groups, and the rise in the vivax series exceeded that in the falciparum series. Differential leucocyte counts in 500 patients on treatments A and B were studied, and no significant difference between these two groups was observed. The high dose of mepacrine in treatment B did not produce any apparent change in the differential leucocyte count.

A study of albuminuria was made in the five different treatment groups and in vivax and falciparum malaria. No correlation was made between albuminuria and mepacrine dosage. The incidence of albuminuria in falciparum infection was 47.5 per cent and in vivax infection 19 per cent. A small number of cases showed persistent albuminuria, but the progressive diminution suggested that the persistence of albuminuria was not related to the type of treatment used. In cases under treatment D, 30 grains each of sodium bicarbonate and sodium citrate was given thrice daily for 7 days during the last stage of mepacrine, and for 2 days after the pamaquin stage had begun, and the urine tested on the second and third mornings of alkali treatment. Seventy-two per cent of the urines was found constantly alkaline. Urine tests were also carried out after pamaquin treatment and the urines were found normal.

Synopsis of findings of the study

(i) The groups of patients receiving the five treatments were reasonably homogeneous as regards race, previous history of malaria, weight and parasite density.

(ii) The five treatments showed no marked difference in the periods required for the control of pyrexia and parasitaemia. In the control of pyrexia, quinine appeared to be slightly more effective than mepacrine in vivax malaria. The reverse was the case in falciparum malaria.

(iii) Irrespective of the treatment used, it took approximately ten and thirty days from the day of admission for the erythrocytes in vivax malaria to regenerate to the level found on admission and to five million red cells respectively. Corresponding figures for falciparum malaria were twenty-five and forty days. These regeneration rates might possibly have been accelerated by hæmatinics.

(iv) No abnormality in total or differential leucocyte counts could be demonstrated as a result of any of the treatments used.

(v) None of the five treatments appeared to have any aetiological relationship to the incidence or persistence of albuminuria.

(vi) The most prominent toxic reaction encountered among the five treatments was vomiting. This symptom showed a moderate and approximately equal incidence in the quinine and heavy mepacrine treatment groups (A and B). It was much less common in the lighter mepacrine treatment groups (C and D). The highest incidence of vomiting occurred in the group (E) receiving a medium dosage of mepacrine which commenced with an initial dose of 0.8 gramme.

(vii) Abnormal mental states were noted among all five treatment groups. In the opinion of the clinician in charge of patients, in only two cases could the mental symptoms be reasonably attributed to mepacrine. In the one case an abnormal mental state developed during treatment for a relapse which had followed the

cessation of a heavy mepacrine treatment. This reaction was moderately severe. The other, which was trivial, occurred on the second day of the treatment employing a medium dosage of mepacrine.

(viii) No untoward results attended the omission of the 'rest period' from the light mepacrine course followed by pamaquin.

(ix) The standard treatment was less effective than the other four in preventing relapses during the observation period. Among the treatments employing mepacrine only, the relapse rate during observation was inversely proportional to the total dosage of mepacrine. Pamaquin given after a light mepacrine treatment appeared to have a definite effect in reducing the relapse rate.

(x) No crescents could be found during the observation period among the cases who had received pamaquin during treatment. Among the patients who had received mepacrine treatment without pamaquin, the incidence of crescents was closely related to the mepacrine dosage, although no such relation was apparent during the first week of treatment.

It was clearly demonstrated that a weak and understaffed medical service cannot efficiently undertake the treatment of malaria, and that inefficiency in this respect is fraught with poor therapeutic results which in turn cause widespread loss of confidence in the plan of treatment and value of drugs. It was further demonstrated, with regard to relapses, that results obtained with a particular malaria treatment in endemic areas in peace time could not be expected to compare with those obtained with the same treatment in hyperendemic areas in war, the difference in results being almost certainly due to the multiplicity of infections acquired in such a short time by so many cases.

Evidence has been provided that a fresh attack of malaria is a debilitating constitutional illness, and that any attempt to return troops to duty shortly after the cessation of the acute phase of such an attack disregards the natural history of the disease and its effect upon the individual.

The 'standard treatment' of malaria has been compared with treatments employing mepacrine rationally and starting with a high initial dosage. In the treatment of acute attacks of uncomplicated malaria irrespective of the infecting species of plasmodium, the differences between the standard treatment and those employing mepacrine only were not great. But the standard treatment appeared to be less effective in preventing short-term relapses of benign tertian malaria.

On the findings of this trial, the following recommendations were made: that quinine be omitted from the routine treatment, that the treatment should consist of mepacrine only, commencing with a moderately high dosage, that the treatment with mepacrine be followed by suppressive mepacrine treatment or a modi-

fication thereof, and that pamaquin be omitted from the treatment.

Summary

A short account has been given of certain problems in malaria therapy which have affected the army campaigning on the eastern frontier of India during the years 1942-44 and of the measures which have been taken to deal

with them under the aegis of the Malaria Research Committee, G.H.Q., India.

Acknowledgments

The writers wish to acknowledge their indebtedness to the Director of Medical Services in India, the Director of Medical Services, 11th Army Group, South East Asia Command, the Malaria Research Committee, General Headquarters, India, and to the medical personnel of all ranks.

Medical News

A NATIONAL HEALTH SERVICE FOR CEYLON

DR. W. G. Wickramasinghe in an article in the Journal of the Ceylon Branch of the British Medical Association (April 1945) outlines a National Health Service for Ceylon on the model of the National Service contemplated in the English White Paper. The article points out that no scheme of agricultural or industrial development can prosper which ignores the care of the healthy and the treatment of the sick among those engaged in these undertakings and that the modern tendency as seen in the United States, England, and in Soviet Russia is to offer a service that is available to all. It is stated that the present Ceylon Health Service, whatever its faults, offers to the great majority of the citizens free indoor treatment in the government medical institutions and to the remainder, however, large their income, the same privilege at an expenditure not exceeding 50 cents a day. In the outpatient treatment, all persons who get less than Rs. 50 p.m. are entitled to free treatment and no person need pay more than Rs. 2 for medical examination as well as for medicines an ideal which many countries are striving for. After mentioning the resemblances and differences between the Ceylon Health Service and the contemplated National Service in England, Dr. Wickramasinghe discusses the improvements necessary at the centre and at the periphery, the availability of medical practitioners, apothecaries service, junior medical service, consultant service, hospital facilities, co-ordinating emergency requirements and future needs, rural hospitals, rehabilitation service, nurses including male nurses, medical education and post-graduate study, etc.

MONTHLY CLINICAL MEETING OF 'THE CALCUTTA SCHOOL OF TROPICAL MEDICINE

THE second monthly clinical meeting at the Calcutta School of Tropical Medicine was held at 4-30 p.m. on Wednesday, the 7th November, 1945. Dr. Ukil showed the skiagram taken after lipiodol administration in the case of bronchiectasis shown at the last meeting, and discussed the matter further. Dr. Sankaran outlined the clinical manifestations of vitamin-A deficiency and demonstrated his apparatus for testing dark adaptation. Colonel Murray demonstrated a case of anaemia in pregnancy, and in the discussion expressed the opinion that there was no clinical entity 'anaemia of pregnancy'. Dr. L. M. Ghosh demonstrated a marked case of solar dermatitis. Dr. J. R. Chatterji presented a case of polycythæmia vera in a child. Colonel Greval showed a case of 'glossitis areata exfoliata' of unknown aetiology. Dr. R. N. Chaudhuri showed a case of pellagra associated with thyroid deficiency which responding to treatment with either or both of thyroid extract and nicotinic acid. Dr. Lowe made a brief statement regarding three cases of typhus recently seen in civilians in the Carmichael Hospital for Tropical Diseases.

On all the cases there was considerable discussion in which many took part, and the views expressed, and

in some cases the diagnosis given, were subjected to criticism.

THE INDIAN JOURNAL OF SURGERY

THE June number opens with an article on urinary calculi in which L. B. Joshi discusses their incidence and aetiology. T. H. Somervell gives many practical points in the treatment of malunited fractures and dislocations. K. S. Nigam and J. K. Sircar describe what they call the cholesterol-tolerance test and its importance in the diagnosis of chronic cholecystitis. P. Rama Rau gives an encouraging account of the results of radiation treatment in cancer of the cervix. S. P. Srivastava recommends rectosigmoidectomy as the treatment of choice in irreducible complete prolapse of the rectum. In the last article C. R. Krishnaswami describes an operation on a patient with chondroma of the scapula.

TUBERCULOSIS IN LUCKNOW

UNDER the auspices of the United Provinces Tuberculosis Association, a survey was conducted in the city of Lucknow by A. J. Faridi and K. N. Shukla to find out the extent of infection among the apparently healthy population. They did Mantoux test on a little over 5,000 individuals—men, women and children taken at random, mostly from the Hindus and Moslems, and found that 71.9 per cent of them reacted to tuberculosis up to a dilution of 1 : 100. The intensity of reaction was marked in 6 to 10 and 11 to 15 years age groups. The rate of infection was a little higher among the Moslems.

PRODUCTION OF CINCHONA IN INDIA. LARGE EXTENSION OF ACREAGE DURING 1944-45

THERE was a large extension of acreage under cinchona during the year 1944-45, states the Report of the Principal Quinine Officer, Government of India, on cinchona and quinine for that year. The Government of Madras worked to a programme of 1,000 acres and the Government of Bengal 400 acres. Most of these areas were close planted with a view to obtaining an early crop.

101,419 lb. quinine sulphate and 62,355 lb. of cinchona febrifuge were added, mainly due to production by the Governments of Bengal and Madras, to the total stocks, and 127,803 lb. quinine sulphate and 43,169 lb. of cinchona febrifuge were issued during the year, the balance of stock on 31st March, 1945, being 205,454 lb. quinine sulphate and 103,352 lb. cinchona febrifuge.

There was also a certain revival of interest in cinchona amongst the planters. One tea estate in Assam has grown cinchona in the plains and this, if successful, may have far-reaching possibilities. In Government plantations and in one of the private estates in the south, work is being done on vegetative methods of production. These are likely to contribute materially to a reduction in the cost of production in future.

THE OPIUM POPPY FIELDS*

THE 1914-18 war was followed by widespread drug addiction because no effective controls were imposed on growers of the opium poppy. This time it is hoped that the danger will be checked in time; and the United States have called on all poppy-growing nations to enter into an agreement to grow only enough opium to meet medical and scientific needs. This amount is estimated at 440 tons; whereas the amount actually grown is said to be 2,647 tons. Despite restrictions on shipping, smugglers in 1944 sent to America from India the largest quantity of opium seized by the customs in the past six years. Addiction is again reported to be spreading, and it is said that stocks of drugs have been built up by traffickers who are waiting for a favourable moment to send them into the United States. Fortunately the opium products sent to the U.S. Forces have been strictly controlled during the war, and there are no large stocks left in unauthorized hands as there were in 1918.

* Copied from the *Lancet*, 1st September, 1945, p. 292.

NUTRITION WORK IN BOMBAY*

WITH the advice and guidance of the Nutrition Committee set up in Bombay in August 1943, the Bombay Government organized a comprehensive nutrition scheme.

Over 170,000 priority consumers, children, expectant and nursing mothers, are enjoying the benefits of a scheme for the supply of milk at concessional rates. A special department has been set up under a milk commissioner to develop the production and to regulate the distribution of milk; it is dealing with the problems of establishing cattle farms and providing machinery for converting whole milk into powder. Preparations are also being made for the issue of separated milk tablets reinforced with vitamins A and D to school children between the ages 5 to 10 years.

About 30,000 to 40,000 pounds of vegetables are being imported daily and sold at 'no profit' prices in the Government ration shops. Poultry farming too has been given an encouraging impetus. Quantities of shark-liver oil are being produced in the Fisheries Department and supplied to the Haffkine Institute for the preparation of concentrate.

* Nutrition. Bulletin No. 10, October 1945. Published by the Department of Food, Government of India, New Delhi.

GOVERNMENT OF INDIA, DEPARTMENT OF FOOD, DEPARTMENT OF LABOUR, NEW DELHI. FEEDING THE WORKER, NO. 3. JUNE 1945

THESE quarterly publications appear to meet an increasing demand for greater knowledge from all parts of India. A new feature of the present number is an easily readable and understood article on 'The science of nutrition', which it is proposed to continue. Among the topics dealt with in this pamphlet the following may be mentioned: general introduction to nutrition; the regional food commissioners of the Government of India; our food to-day, model small-size factory canteen; are national restaurants possible; and the facts about milk.

NUTRITION*

THIS brochure contains short popular notes on vitamins, minerals, gardening, etc. In 'building a nation' the importance of school feeding is stressed, but the main obstacle is its cost. An officer has already been appointed by the Central Food Department to investigate the subject and make constructive

suggestions in consultation with the existing schemes in Cochin, Ceylon and Madras. Since the milk supplies of India are inadequate, it is worth considering the possibility of importing dried separated milk powder from Australia and New Zealand, if available at cheap cost, for use in school feeding.

* Nutrition. Bulletin No. 11, November 1945. Published by the Department of Food, Government of India, New Delhi.

CARBON MONOXIDE: ITS HAZARDS AND THE MECHANISM OF ITS ACTION*

THE Federal Security Agency of the United States Public Health Service, Washington, has published a report on the various aspects of carbon monoxide poisoning, the mechanism of its action and the methods of treatment. Prompt elimination of carbon monoxide from the organism, best accomplished by the administration of oxygen, is considered to be of great importance. The value of simultaneous administration of carbon dioxide has been discussed and its potential dangers have been pointed out. Among other therapeutic measures, venesection, lumbar puncture and intravenous injections of hypertonic solutions have been found successful in reducing oedema of the brain, while the use of morphine and atropine is contra-indicated. It is hoped that this synopsis will stimulate further research on the various phases of the problem.

* Being a report published in the *Public Health Bulletin*, No. 290.

NOTIFICATION OF TUBERCULOSIS IN ENGLAND*

THE Committee on Notification of Tuberculosis proposed some important changes in the present system. The most notable is a suggestion that notification in the future be a two-stage procedure. The first stage would be that of intimation. A practitioner, suspecting that a patient might be tuberculous, would be able to send a non-committal intimation to the local authority instead of, as now, being compelled to make up his mind and decide upon a definite diagnosis of tuberculosis, which automatically puts the patient on the register of tuberculous persons. Under the new procedure, the final diagnosis of the patient, and therefore the responsibility of placing him on the register, would rest with the tuberculosis officer. At the same time, there would be nothing to prevent the general practitioner who was certain of his ground from notifying the patient exactly as is done now. The value of the suggested new system would be that provision would be made for the doubtful case, whose illness could be thoroughly investigated by a tuberculosis consultant without any possible 'registration stigma' in the event of his turning out not to have the disease.

* Abstracted from the *Medical Officer*, 22nd September, 1945, p. 94.

FIRST INDIAN CONGRESS OF RADIOLOGY

THE First Indian Congress of Radiology will be held at Madras from the 13th to 16th February, 1946, under the Presidentship of Dr. M. D. Joshi, M.B., B.S. (Bom.), D.M.R.E. (Camb.), F.C.R.S. (Bom.), J.P., Bombay. Four sections dealing with X-Ray Diagnosis, Radiotherapy, Radiation Physics and Radio Biology will be a feature of this Congress under the Chairmanship of Dr. S. C. Sen (Delhi), Dr. K. P. Mody (Bombay), Dr. R. Naidu (Bombay), Dr. V. R. Khanolkar (Bombay) or Dr. Bhaskara Menon (Vizagapatam), respectively. These sections will be consecutively held

at the general sessions of the Conference. Each section will open with an address by its Chairman who will give his opening address. Papers will then be read, discussion will follow and the Sectional Chairmen will wind up their respective sections. The President of the Congress will deliver his Presidential Address at the inauguration meeting and will wind up the whole session with his concluding remarks. This Congress is held under the auspices of the Indian Radiological Association.

There will also be a Scientific Exhibition which will include interesting radiographs with case notes and surgical or post-mortem findings thereon and will be exhibited on viewing boxes. Therapy charts, follow-up results, and radiographs of normal and abnormal post-mortem specimens will also be exhibited.

Those who are interested in attending this Conference are kindly requested to get in touch with the General Secretary, Dr. P. Rama Rao, 155-157, Poonamallee High Road, Kilpauk, Madras.

FACULTY OF TROPICAL MEDICINE AND HYGIENE, BENGAL

THE following students are declared to have passed the L.T.M. Examination, session 1945.

Passed

(Arranged in alphabetical order)

1. Dr. Bhagwan Swarup, L.C.P. & S. (Bomb.), Sub-Assistant Surgeon, Victoria Hospital, Ajmer.
2. Dr. Govind Trimbak Bhat, L.C.P. & S. (Bomb.), Private Practitioner.
3. Dr. Sachindra Lal Chakraborty, L.M.P. (Assam), Private Practitioner.
4. Dr. Madan Mohan Das, L.M.F. (Bengal), Assistant Clinical Pathologist, Chittaranjan Hospital, Calcutta.
5. Dr. Bhaskar Vithalrao Deshmukh, L.M.F. (Bengal), Private Practitioner.
6. Dr. Chandrashekhar Damodar Deshpande, L.M.F. (Bengal), Private Practitioner.
7. Dr. Rama Shanker Dube, L.M.P. (C. P.), Private Practitioner.
8. Dr. Mohan Lal Gupta, L.M.P. (C. P.), House Surgeon, King Edward Hospital, Indore.
9. Dr. Rama Nand Jain, L.S.M.F. (Punjab), Health Officer, Municipal Committee, Sangrur, Jind State.
10. Dr. Niroj Mohon Lahiri, L.M.F. (Bengal), Private Practitioner.
11. Dr. Lalchand Gopaldas Marda, L.C.P. & S. (Bomb.), Private Practitioner.
12. Dr. Sailendra Nath Mitra, L.M.F. (Bengal), Private Practitioner.
13. Dr. Mohammed Akhtar Khan, M.B., B.S. (Punjab), Private Practitioner.
14. Dr. Gajanan Balkrishna Mudafale, L.M.P. (C. P.), Assistant Medical Officer, Amraoti, C. P.
15. Dr. Janamejay Mukerji, L.M.F. (Bengal), Private Practitioner.
16. Dr. Sudhir Kumar Pal, L.M.F. (Bengal), Assistant Medical Officer, Dalmore Tea Estate, Dooars.
17. Dr. Ramendra Kishore Sarma Biswas, L.M.F. (Bengal), Assistant Medical Officer, Gouripur Charitable Dispensary, Mymensingh.
18. Dr. Birendra Mohan Sinha, L.M.P. (Bihar), Medical Officer In-charge, Jamira Dispensary, Shahabad.

PALUDRINE (M 4888) IN MALARIA

RESULTS of experiments with Paludrine (known as M 4888 during the war) have been reported.

The efficacy of the drug for human beings had been proved on 200 Australian soldiers who volunteered as

patients at a medical research unit at Cairns, Northern Queensland. Brigadier N. Hamilton Fairley was in charge of experiments, assisted by a large team of research workers, including physicians, pathologists, and entomologists.

The first important result obtained at Cairns has been to show that in malignant malaria paludrine destroys parasites inoculated by the infected mosquito at an early stage of their development.

In consequence, the parasites never gain access to blood circulation. If three tablets (each 1/10 gm. or 1½ grains) of paludrine be swallowed three hours before the volunteer is bitten by as many as ten heavily infected anopheline mosquitoes, malignant tertian malaria does not occur. Paludrine is thus a true causal prophylactic and is far more effective than either quinine or atebine under identical circumstances.

Volunteers in the Cairns test were subjected to repeated malaria infections, and to long marches in hilly country and to extremes of climate. Despite these and other stresses, they remained amazingly fit, although under tests they were bitten by as many as 200 infected mosquitoes.

If volunteers taking one tablet of paludrine daily be bitten by mosquitoes infected with benign tertian malaria, they fail to develop any symptoms of malaria, or show any malaria parasites in the blood while paludrine is being taken. One tablet has proved sufficient to end an attack and bring temperature to normal in both malignant tertian and benign tertian infections. Nothing like this can be achieved by either quinine or atebine. However, it is pointed out that it is too early yet to assess the ultimate cure rate in benign tertian malaria.

Results at Cairns suggest that the mere taking of one or two tablets each week-end would give complete freedom from attacks.

(Abstracted from Release No. P/255 of the Public Relations Officer, Australian High Commissioner's Office, Delhi.)

FOOD YEAST

A SURVEY of the nutritive value of food yeast by the Accessory Food Factors Committee of the Medical Research Council* has shown results which are summarized below:

1. Food yeast contains proteins, in amount equal to about half its dry weight, which, when included in a diet of which the protein is otherwise derived mainly from cereals, possess a high nutritive value, approaching that possessed by milk proteins.

2. Like other types of yeast, food yeast is one of the richest known sources of B vitamins, including vitamin B₁, riboflavin and nicotinic acid; in this respect it is rivalled only by liver, the values being calculated on a dry weight basis.

3. Dried food yeast has been found to be an acceptable and generally palatable food for human subjects, both children and adults. Taken in small amounts, ½ to 1 oz. (3 to 14 g.) daily, it provides a valuable addition to the B vitamins contained in an ordinary diet. In one trial with children, consumption of 8 g. of dried food yeast daily in a biscuit distributed on 5 days weekly was associated with an improved rate of increase in weight. A daily dose of 3½ g. was given with benefit to a group of children suffering from gingivitis.

4. About ½ oz. of dried food yeast may be regarded as a maximum adult daily dose in ordinary circumstances; ½ oz. daily may be taken without any risk of digestive disturbance.

5. In Nigeria, subjects with symptoms of deficiency of B₂ vitamins have shown striking improvement, or cures, after 5 to 7 weeks' treatment with 4 to 7 g. of food yeast daily.

* M.R.C. War Memorandum No. 16. Food Yeast: A survey of its nutritive value. London: H. M. Stationery Office, 1945. 3d. net.

Public Health Section

DISPOSAL OF NIGHT-SOIL AND RUBBISH BY COMPOST SYSTEM

By B. L. CHOPRA, L.B.C.P., L.R.C.S., L.R.F.P.S. (Edin.),
D.P.H., D.T.M. (Eng.), L.M. (Dub.)

Divisional Medical Officer, N. W. R., Ferozepore

THE preparation of compost manure from farm and habitation wastes is an age-old practice with the Chinese, but the real systematization of the process started with the work of Russel and Hutchinson who evolved the ADCO process for the preparation of compost manure from farm wastes at Rothamsted in 1917. Composting of refuse and night-soil was first started in India by Fowler by the so-called activated compost process or by the Mysore method in 1930, and by Jackson by the Indore process in 1932. In the process recommended by the latter, compost preparation is done on special platforms, but the system has not become popular due apparently to the fly and smell nuisance. In parts of Bengal the composting of night-soil and rubbish with dried water hyacinth on that large quantity of manure rich in organic

and nitrogenous matter should be made available. Dr. M. R. Madhok conducted a class of sanitary inspectors at Ludhiana in July 1944. Due to the rights of night-soil contractors at Ludhiana, it was not possible to get material for experimental compost pits at that station. We, however, asked the railway night-soil contractors to provide the material for Dr. M. R. Madhok's demonstrations for teaching his class; the contractors agreed and pits 14 feet long, 7 feet wide and 3 feet deep were dug. Each pit was filled with the following 3 layers: 9 inches of rubbish from dust bins and 3 inches of night-soil emulsion, and then again 9 inches of rubbish and 3 inches of night-soil and then finally a 3rd layer similar to the above two.

The top layer was 9 inches dry refuse. The pit was then covered with a layer of more than 2 inches of dry earth and a bund made all around to divert any rain water. Night-soil and rubbish were allowed to stay in the pit for four months. A sample of the manure was then sent for analysis which yielded the following results:—

1	2	3	4	
Moisture (per cent)	Additional moisture to oven dry basis (per cent)	Stone and gravel on oven dry compost sample (per cent)	ANALYSIS OF THE PORTION FREE FROM STONES AND GRAVEL (OVEN DRY BASIS)	
			Loss on ignition	Nitrogen
31.0	4.63	8.10	16.11	0.70

concrete platforms, however, has been very successful.

My attention was first drawn to the Bangalore method of compost preparation by Dr. M. R. Madhok, Provincial Biochemist (Compost), Punjab. For the purposes of the 'grow more food campaign', it was essential

Dr. M. R. Madhok however thought that actual figures for nitrogen should be much higher because the sample sent for analysis was by mistake sieved through a fine mesh sieve and therefore much of the organic matter was left out. Another sample was then sent and the results of analysis are as follows:—

1	2	3	4	
Moisture (per cent)	Additional moisture to oven dry basis (per cent)	Stone and gravel on oven dry compost sample (per cent)	ANALYSIS OF THE PORTION FREE FROM STONES AND GRAVEL (OVEN DRY BASIS)	
			Loss on ignition	Nitrogen
32.0	5.0	10.0	17.0	1.7

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The advantage of this system over old trenching of night-soil is that it yields much more manure rich in organic matter and nitrogenous contents, and the night-soil and refuse are satisfactorily disposed of without any nuisance. The same pits become available after four months when manure is taken out for sale or use in cultivation plots. The only disadvantage that has come to my notice is that whilst filling the pit with alternate layers of night-soil and refuse, wind carries the smell to places nearby if on the windward side. Once the pit is closed no nuisance is ever complained of.

This compost system has now been introduced by me in the railway colonies at all big stations in the Ferozepore division like Ferozepore, Pakpattan, Kasur and Bahawalnagar. Work is being carried on without any nuisance. Even during

the monsoon months this system has worked most satisfactorily, and we are this month selling by auction the following quantity of compost manure:—

1. Ferozepore 10,198 cubit feet.
2. Bahawalnagar 5,966 cubit feet.
3. Kasur 7,976 cubit feet.

This system is well worth a trial where a simple and inexpensive system is to be tried. On the B. B. & C. I. Railway in the Bombay area, which is damp, composting of night-soil on concrete platforms is in vogue, and is reported to work very well.

My thanks are due to Dr. C. D. Newman, Chief Medical and Health Officer, and to Divisional Superintendent, Ferozepore, for the great encouragement and support I am deriving from both for conducting these experiments.

Current Topics

Streptomycin for Typhoid

By H. A. REIMANN

W. F. ELIAS

and

A. H. PRICE

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXVIII, 19th May, 1945, p. 175)

STREPTOMYCIN, a non-toxic antibiotic substance derived from *Actinomyces griseus*, when injected intravenously or intramuscularly in doses of from 1 million to 4 million units daily appears in the blood and urine in patients with typhoid in amounts theoretically sufficient to kill *E. typhosa*. Small quantities are excreted in the faeces. When given orally, only traces appear in the blood and urine, and most of it is excreted unchanged in the faeces in quantities excessive to suppress *E. typhosa* and *E. coli*. Both parenteral and oral therapy seem to be desirable in treating typhoid, the one to control systemic and urinary tract infection, the other to sterilize the faeces, to prevent reinfection and to avoid the carrier state. There is evidence that different strains of *E. typhosa* vary in their resistance to streptomycin, but there is no evidence here of the development of increased resistance to streptomycin during exposure to it in the body.

Of 5 patients treated parenterally with streptomycin, recovery took place in 3 during treatment.

Mass Sulphadiazine Prophylaxis of Respiratory Diseases in the U. S. Navy

By A. F. COBURN

(Abstracted from the *Bulletin of the New York Academy of Medicine*, Vol. XXI, June 1945, p. 281)

SULPHADIAZINE prophylaxis has been administered to approximately 600,000 Naval personnel and approximately 300,000 similar personnel have been observed as controls.

The institution of this measure was followed by a marked reduction in the morbidity rates for respiratory diseases.

The incidence of respiratory symptoms observed at sick call was significantly lowered.

Hospital admissions for respiratory diseases were reduced from rates varying between 5 and 18 per 1,000 per month to less than 1 per 1,000 per month.

Meningococcal infections were eliminated.

The incidence of pneumococcal pneumonia was significantly lowered at most Naval stations.

Morbidity rates for respiratory diseases caused by filtrable viruses were unaffected.

The most effective dosage tested was 1.0 gramme daily.

The administration of 0.5 gramme of sulphadiazine daily was also found effective and was followed by fewer untoward reactions.

Mild, untoward drug reactions were observed in about 0.5 per cent. Severe reactions occurred in 0.01 per cent of men taking 1.0 gramme of sulphadiazine daily.

Sensitization of Naval personnel to sulphonamides and the development of sulphadiazine-fast respiratory pathogens did not occur.

Pneumonic Plague

By E. J. MUNTER

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXVIII, 26th May, 1945, p. 281)

A CASE of primary pneumonic plague was contracted accidentally during laboratory research. The nature of the illness was recognized within twenty-six hours after its acute onset, and therapy with sulphadiazine was instituted at once. The patient had received a large amount of plague vaccine a year previous to the illness. He was placed in an oxygen tent promptly on admission to the hospital as a therapeutic and as a quarantine procedure, and other strict quarantine practices were carried out. Secondary cases did not occur. The patient recovered.

Single Injection Treatment of Gonorrhoea with Penicillin in Beeswax-Peanut Oil

By CAPTAIN M. J. ROMANSKY, et al.

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXVIII, 9th June, 1945, p. 404)

1. ONE hundred and seventy-five cases of gonorrhoea in males were treated by a single injection of calcium penicillin in beeswax-peanut oil. There were

no failures among 75 patients receiving a single injection of 150,000 units. Ninety-three of the 100 patients who received a single injection of 100,000 units were cured. The remaining 7 who received 100,000 units were failures and responded to a second single injection of 150,000 units of penicillin in beeswax-peanut oil.

2. A single injection of 100,000 to 150,000 units of calcium penicillin in beeswax-peanut oil will produce and maintain assayable levels of penicillin in the blood for seven-and-a-half to ten hours, with excretion of penicillin continuing in the urine for twenty-four to thirty-two hours.

3. The penicillin in beeswax-peanut oil mixture has produced no abnormal reactions locally or constitutionally.

Nutritional Macrocytic Anæmia and the Animal Protein of Diet

By G. F. TAYLOR

and

P. N. CHUTTANI

(Abstracted from the *British Medical Journal*, i, 9th June, 1945, p. 800)

A FULL blood investigation of 50 consecutive cases of anæmia in Indian men in an extreme desert climate, where there was a low sickness rate (about 1.5 per 1,000 per day), showed that the admission rate to hospital for anæmia per 1,000 of population among vegetarians was 22 times greater than among meat-eaters. The incidence of severe anæmia was very much greater in vegetarians than in meat-eaters in this series.

The anæmia differed in type and severity in the two groups, being mainly macrocytic in the vegetarians (nutritional or tropical macrocytic anæmia) and hypochromic and either normocytic or slightly microcytic in the meat-eating group. No case of nutritional macrocytic anæmia was seen in a meat-eater.

In all cases except one, a complicating factor was found, hookworm and malaria being most frequent.

The difference in the habits of the two groups, which were otherwise alike, was that social customs prevented the vegetarian group from eating the weekly ration of 20 oz. of fresh mutton in the meat-eaters' ration. The absence of this meat appeared to be the cause of macrocytosis and severity and frequency of anæmia in the vegetarian group. The rations contained over 3,000 calories and over 80 g. of vegetable protein. Riboflavin and vitamin A were known to be low.

It will be of interest to compare these results with findings when the stress of severe frequent malarial infection and dysentery is great.

One case showed that a severe macrocytic anæmia may develop within three months if milk, fresh fruit and vegetables are much reduced in a vegetarian diet. Another case in which severe macrocytic anæmia developed during a prolonged fever (undulant fever) showed the need of liver and iron in the diet in cases of chronic illness.

SUMMARY

The incidence, type, and severity of anæmia in an Indian adult male population of about 18,000 were shown to depend on the meat content of the diet. Nutritional macrocytic anæmia occurred only in vegetarians in a series of 50 cases.

Eosinophilia Caused by Atabrine

By H. K. RUSSELL

(Abstracted from the *United States Naval Medical Bulletin*, Vol. XLIV, March 1945, p. 574)

ONE hundred and twenty patients on atabrine therapy for malaria showed an average eosinophilic count of 8.4 per cent. Fifty men on suppressive treatment with atabrine sufficient to produce a distinctly

yellow colour of the skin showed an average eosinophilia of 7.2 per cent. Thirty-three men who had not taken atabrine and were clinically free from malaria showed an average eosinophilic count of 3 per cent.

It seems probable that atabrine in sufficient amount to produce a yellow colour of the skin will stimulate an eosinophilic hyperplasia of the bone marrow and a moderate eosinophilia in the peripheral blood.

Meniere's Syndrome

(From the *British Medical Journal*, ii, 14th July, 1945, p. 52)

THE clinical diagnosis of Ménière's syndrome is nearly always easy, but the pathological basis of the lesion or stimulus which brings on these attacks is still unknown. A number of temporal bones have now been examined, and in some gross dilatation of the membranous labyrinth has been demonstrated; nevertheless we do not know the mechanism by which the labyrinthine storm is raised, and consequently treatment is empirical, such as destruction of the labyrinth or section of the eighth nerve. Shelden and Horton based a method of treatment on the idea that alteration in the permeability of the capillary walls with local oedema is the probable aetiological factor, without specifying whether the oedema is likely to be intracellular or extracellular, and histamine was suggested as an agent which would perhaps affect capillary permeability. In 1940 and 1941 they reported spectacular relief in certain cases by the intravenous injection of histamine. Now Lillie, Horton and Thornell present a review of 25 cases treated by injection of histamine but studied from a slightly different aspect. Of these patients 18 were men and 7 women, and their ages ranged from 27 to 65 years, with an average of 46. The treatment consisted in the intravenous injection of 2.75 mg. of histamine diphosphate (the equivalent of 1 mg. of histamine base) in 250 c.cm. of either normal saline or 5 per cent solution of dextrose or 0.8 per cent solution of potassium chloride, at the rate of 20 to 60 drops a minute. The administration was repeated daily for three to six days. Subcutaneous injections were also given consisting of a 1 to 10,000 solution of histamine base, the dosage rising gradually by 0.05 c.cm. from 0.2 c.cm. to 1.0 c.cm. Audiometric studies of this series of cases showed that in 12 of the 25 the hearing was improved by the treatment, and in 6 of these the improvement was very noticeable. In 4 of these 6 the potassium chloride solution was used. Tinnitus was present in all but one case. In 10 there was no change, but in 2 cases the tinnitus disappeared, and it was much improved in 8. Vertigo was the symptom which showed the best response, for it disappeared completely in 19 cases, and in only 2 was there no change. These observers were not able to confirm the suggestion made by Atkinson that such cases could be divided by intradermal testing into those sensitive to histamine. By such a selection of cases those insensitive to histamine could be treated in some other way, and Atkinson proposed the administration of nicotinic acid for its vasodilator effect, not for its action as a vitamin. Regarding tinnitus as a form of paresthesia, Atkinson has claimed that all vasodilators bring transient relief—an effect which can be produced by blocking the stellate ganglion or injecting drugs with vasodilator action. Using nicotinic acid as the vasodilator, he claims a high percentage of good effects in all forms of deafness accompanied by tinnitus.

From all this it appears that the control of the labyrinthine circulation may prove to be the factor in the successful treatment of Ménière's syndrome, but it is probably the circulation of the endolymph, rather than the vascular circulation, which needs to be controlled. However, very little is known about the endolymph, though by analogy it is probably secreted by the capillaries in the stria vascularis in the cochlea in the same way as the cerebro-spinal fluid is secreted by the choroid plexus. The endolymph is probably

secreted also from capillaries in the sacculi and utricle and in the semicircular canals, but nothing is certain about this. It remains also to determine how the effect can be maintained in persons who respond favourably to histamine, and the continuation of maintenance doses by subcutaneous injections is suggested. This line of management is supported by the success which sometimes attends simple restriction of salt intake, the sodium ion being considered the morbid factor. Large doses of ammonium chloride are used to replace the salt—45 grains in capsules three times a day with meals. The success attending the small number of cases in which the histamine was given in a solution of potassium chloride is perhaps significant. There will, however, remain a proportion of cases in which the function of the labyrinth is so disordered that the symptoms will yield only to destruction of the labyrinth or section of the eighth nerve. Lillie, Horton and Thornell give an excellent bibliography of the whole subject, of which the above commentary displays only one facet.

Fractionation of Blood Proteins

(Abstracted from the *International Medical Digest*, Vol. XLVI, March 1945, p. 184)

STUDIES on the fractionation of blood had been started in the Department of Physical Chemistry at Harvard Medical School by grants from the University and the Rockefeller Foundation, and when the need for these by-products increased so rapidly, because of the war, the National Research Council and other agencies furnished the means of hastening this work to a conclusion. What has been accomplished has been described fully in previous articles. In brief, this extraordinarily co-ordinated investigation has already yielded normal human serum albumin for use in shock and burns; isohæmagglutinins for use in blood grouping; thrombin used with fibrinogen for the formation of clots in certain surgical conditions including skin grafting; fibrin and fibrinogen tubes and plastics which may prove useful in surgery; fibrin films used as a covering for burns and as an artificial dura in brain surgery, and the immune serum globulins, the fractions responsible for the effectiveness of pooled serum or convalescent serum in modifying or preventing contagious diseases.

Effect of Vitamin B₆ (Pyridoxine) in the Treatment of Leucopænia and Granulocytopenia of Toxic Origin in Humans: Preliminary Report

By M. M. CANTOR

and

J. W. SCOTT

(From the *Science*, 15th December, 1944, p. 545, as abstracted in *Bulletin of Hygiene*, Vol. XX, May 1945, p. 271)

PYRIDOXINE hydrochloride was given in daily doses of 125 to 200 mg. for 5 to 6 days to three patients who had agranulocytic angina. The condition followed medication with sulphathiazole in the first patient, and showed no improvement after repeated blood transfusions and large doses of pentose nucleotide. When treatment with pyridoxine was started, the leucocyte count was 2,850 per c.mm. and granulocytes were absent from the peripheral blood: with two days the leucocytes had risen to 8,050 with 44 per cent of granulocytes; improvement in the blood picture continued and a leucocytosis of 28,000 was obtained.

No chemical cause apart from aspirin was known for the condition in the second patient, whose condition showed no improvement after one transfusion of whole blood. The response to pyridoxine was similar to that in the first patient.

The third patient developed the condition after two months' treatment with thiouracil for hyperthyroidism. Only pyridoxine was used in the treatment; the original leucocyte count was 4,300 per c.mm. with 6 per cent of granulocytes; in two days the leucocytes were 5,400 with 30 per cent of granulocytes, the percentage of granulocytes continued to increase during the next week but no leucocytosis developed.

In all three cases the temperature fell to normal limits and the symptoms disappeared within 48 hours.

[If these results are confirmed, they represent an important contribution both to the therapy of a most worrying condition and to the elucidation of the physiology of the bone marrow.]

The Treatment of Subacute Bacterial Endocarditis

(Abstracted from the *New York State Journal of Medicine*, Vol. XLV, 1st July, 1945, p. 1452)

SUBACUTE bacterial endocarditis was found almost uniformly fatal until a few years ago. With the use of the sulfa drugs, disappearance of the bacteræmia became a fairly common experience and occasional patients (4 to 6 per cent) were completely cured. The early experiences with penicillin were quite discouraging. The use of massive doses of penicillin has brought this disease under control. Some regard heparin as an important adjuvant and recommend its subcutaneous injection in a special menstruum which retards absorption. The causative organisms of this disease vary widely in their susceptibility to penicillin, and for the more resistant cases para-aminohippuric acid given together with penicillin offers some promise of providing more effective penicillin blood levels. Some prefer the intravenous route. Others have obtained satisfactory results by the intramuscular route. There still remains much to be done in order to establish the most effective dosage and method of administering, but the fact seems fairly clear that 4 out of every 5 patients with subacute bacterial endocarditis may now look forward to a cure.

Fatal Cardiac Tamponade Following Sternal Puncture

By J. H. SCHERER

and

J. S. HOWE

(Abstracted from the *Journal of Laboratory and Clinical Medicine*, Vol. XXX, May 1945, p. 450. As abstracted in *Journal of the American Medical Association*, Vol. CXXVIII, 4th August, 1945, p. 1051)

SCHERER and Howe report the history of a man aged 31 in whom several unsuccessful attempts were made to aspirate marrow from the sternum. The depth to which the needle was inserted at times reached about 3 inch. Repeated attempts at several levels resulted only in the aspiration of a small amount of blood-tinged fluid. The procedure was given up as unsuccessful. Shortly thereafter the patient became pale, semicomatose, breathing noisily and with pupils dilated. The pulse was thready and rapid and the blood pressure not determinable. The foot of the bed was elevated, nikethamide and epinephrine were given and artificial respiration was started. The patient died suddenly after a few minutes, approximately thirty minutes after the unsuccessful aspiration. Necropsy revealed a through and through needle puncture wound of the sternum just below the sternal angle, with slight periosteal extravasation of blood about the point of exit on the posterior surface of the sternum. Directly beneath this wound there was a similar needle puncture wound through the parietal pericardium. The pericardial sac was distended by approximately 350 c.c. of fresh blood, and the heart was completely surrounded

by fresh clot. Just beneath the puncture wound of the parietal pericardium there was a triangular laceration of the musculature of the right ventricle 1 cm. in greatest diameter. The authors say that this is the second death from sternal puncture recorded in the literature and the first reported necropsy on such a case.

Dengue Vaccine

(From the *Journal of the American Medical Association*, Vol. CXXVIII, 4th August, 1945, p. 1026)

THANKS to the heroic co-operation of inmates of the New Jersey State Prison, who volunteered without offer of reward to serve as subjects for numerous inoculations with virus, Sabin and his associates of the Army Epidemiological Board announce the development of a promising new vaccine for dengue virus.

In 1928 Maoussakis found that dengue virus (infective human serum) which had lost its pathogenicity as a result of irradiation, heating or prolonged storage would not protect non-immune human beings against subsequent inoculation with a non-viable dengue vaccine was without promise as a prophylactic measure. Blanc and his associates of the Hellenic Pasteur Institute subsequently found that repeated vaccination with a dengue vaccine (infectious serum) attenuated by the addition of 5 to 8 per cent bile confers an effective immunity. Such an unstable vaccine was of little practical promise. Equally unsuccessful attempts to prepare an attenuated vaccine made with individual bile salts, formaldehyde, chloroform, phenol and other chemical agents.

These earlier failures narrowed the search for a practical dengue vaccine to the possibility of developing a natural human virus of sufficiently low virulence or an antigenically similar virus from lower animals. Evidence was not available, however, that any wild or domestic animal contracts dengue naturally during an epidemic, in spite of the probability that many are bitten by infective mosquitoes. Attempted experimental inoculation of domestic animals also gave negative results. Guinea-pigs inoculated intraperitoneally with massive doses of infected human blood may at times harbour the virus for as long as nine days without febrile response or other evidence of illness. Inoculation from these animals into other guinea-pigs, however, failed to show a continuation of the cryptic infection.

In 1931 Dinger attempted without success to propagate the dengue virus by intracerebral inoculation into young mice, using infective human serum as the inoculum. In the New Jersey prison experiments this technique was varied by inoculating young mice intracerebrally with an ultra-centrifuged concentrate of such serum, this concentrate containing approximately 10 million minimum human infective doses per cubic centimetre. On the first attempts only 10 to 20 per cent of the inoculated Swiss mice exhibited clinical signs of infection and then only after an incubation period of nearly four weeks.

Serial passage was accompanied from these few first generation mice, 0.2 c.c. of a 5 per cent centrifuged suspension of brain and cord being used as the inoculum. As a result of murine serial passage there was a definite increase in the virulence for mice of the dengue virus. By the sixth passage the incubation period had been reduced to two weeks, and the incidence of fatal paralysis increased to approximately 60 per cent. By the ninth passage the fatalities were still further increased to 90 per cent and by the fifteenth passage to 100 per cent.

The virus, however, did not acquire a pathogenicity for cotton rats, guinea-pigs, hamsters or rabbits. Its human pathogenicity was greatly reduced. Up to the fifth passage 0.2 c.c. of a 1:1,000 dilution of centrifuged mouse brain and cord suspension produced skin

lesions at the site of intracutaneous injection in human volunteers. This was followed six to nine days later by fever, maculopapular and petechial rash, leucopenia and enlargement of certain lymph nodes. Infective concentrations of the virus were demonstrable in the blood of the inoculated volunteers, and transmission by *Aedes aegypti* mosquitoes was accomplished. A solid convalescent immunity to subsequent infection with fully virulent dengue virus invariably followed this inoculation.

By the tenth passage subcutaneous injection of fifty times this routine dose usually gave rise to no systemic reactions in the human volunteers, there being at most only a slight fever without headache or malaise lasting less than twenty-four hours. When the same multiple dose was given simultaneously or mixed with the regular U.S. Army dose of yellow fever vaccine, even these occasional symptoms were rarely noted, presumably because of the well-known 'interference phenomenon' between heterologous viruses. All human volunteers inoculated with the practically avirulent tenth mouse passage dengue virus acquired a solid immunity against bites of mosquitoes from a batch of mosquitoes demonstrably infective to non-immune human volunteers. Volunteers immunized with the combined dengue-yellow fever vaccine also developed neutralizing antibodies for the yellow fever virus.

From these preliminary successes Sabin concludes that mouse-adapted dengue virus could be used safely and effectively as a prophylactic vaccine against dengue fever. Whether or not a polyvalent vaccine would be required has not yet been determined. If this murine dengue vaccine proves clinically successful, the War Department would be fully justified in awarding suitable recognition to each inmate of the New Jersey State Prison who volunteered for the experimentation.

Transmission Experiments in Serum Jaundice and Infectious Hepatitis

By J. R. PAUL, et al.

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXVIII, 28th July, 1945, p. 911)

TRANSMISSION experiments in man have enhanced our knowledge of serum jaundice and infectious hepatitis.

In serum jaundice the interval between inoculation and the development of symptoms is usually relatively long, averaging from sixty to one hundred and twenty days.

The agent (or 'virus') of serum jaundice is in the blood during active stages of the disease and also during the interval between inoculation and the onset of jaundice.

Experimental work indicates that the agent or agents of serum jaundice and of infectious hepatitis are quite similar, as is also the clinical picture of the disease produced, resembling, as it does, the picture of catarrhal jaundice.

The agent or agents of serum jaundice and of experimental hepatitis are both filtrable and both relatively resistant to heat.

A prominent difference between serum jaundice and infectious hepatitis, yet to be explained, lies in the length of the incubation period, which may be quite variable, but in our experimental cases of infectious hepatitis it tended to be from eighteen to thirty days, in contrast to the sixty to one hundred and twenty-day incubation period of experimental cases of serum jaundice.

Three patients who had recovered from serum jaundice six months before were not found to be immune to experimentally induced attacks of infectious hepatitis. However, little is known regarding immunity in infectious hepatitis, and the case with which these three patients were 'reinfectured' is not regarded

as an indication that the two diseases are fundamentally different.

The virus of infectious hepatitis is in the blood and in the faeces during active stages of the disease.

Infectious hepatitis can be readily produced in man by the oral route. This can be accomplished by feeding infective faeces or by spraying such material into the nasopharyngeal passages. Similarly the disease can be produced by feeding infective serum as well as by its parenteral administration.

The Methylene Blue Test in Infectious (Epidemic) Hepatitis

By S. S. GELLIS

and

J. STOKES

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXVIII, 14th July, 1945, p. 782)

THE modified methylene blue test for bilirubin in the urine employed in a study of infectious (epidemic) hepatitis with jaundice proved of value (a) in the early diagnosis of preicteric hepatitis, (b) in evaluating the course of the disease and (c) in the prediction of impending relapse. Because of the simplicity of the test, it appears most useful in large scale testing during the course of an outbreak of infectious hepatitis and in installations where complete laboratory facilities are lacking.

The Hyperæmia Effect of Gonadotropins on the Ovary and Its Use in a Rapid Pregnancy Test

By B. ZONDEK, *et al.*

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXVIII, 28th July, 1945, p. 939)

1. CHORIONIC gonadotropin brings on, in the ovary of rodents, the well-known anterior pituitary reactions (I-III). The earliest of these reactions is hyperæmia of the ovary of the infantile rat. Hyperæmia occurs as early as two to six hours after injection, reaches its peak after twenty-four hours and disappears in forty-eight hours. Hyperæmia is the first stage of anterior pituitary reaction II, its second stage being the follicle hæmorrhage (blood dot).

2. Hyperæmia of the ovary does not appear in all rodents in a similar way. The infantile rat is the best reactor, whereas the infantile mouse and rabbit cannot be used.

3. As regards the hyperæmia effect (anterior pituitary reaction II) in the rat, the gonadotropic hormone from the anterior pituitary lobe is the most active, pregnant mare blood-gonadotropin is the least active, and the activity of chorionic gonadotropin from pregnancy urine lies in between. With chorionic gonadotropin hyperæmia may be produced with the same amount of hormone which evokes vaginal œstrus; the amount used for luteinization is about three times as great.

4. Hyperæmia is apparently evoked by the luteinizing hormone, while the follicle stimulating hormone seems to play a rôle as an augmenting factor.

5. The hyperæmia hormone pregnancy test in the infantile rat may be used for the early determination of pregnancy. The time factor plays a decisive part. In the two-hour test the reaction is extremely unreliable, so that the pregnancy can be diagnosed in only 69 per cent of the cases and with the six-hour test in 92.2 per cent, whereas the twenty-four-hour test is reliable in 100 per cent of the positive cases. There may be, however, occasional positive results with the twenty-four-hour test with non-pregnant patients (tumours). They bring the error in the twenty-four-hour test to 1 per cent (tested in 300 cases). The two- and six-hour tests can be relied on if the result is

positive. When it is negative, the result of the twenty-four-hour test must be awaited.

6. The hyperæmia test in the infantile rat is suitable in undisturbed pregnancies. In cases of disturbed pregnancies (ruptured extra-uterine pregnancy, threatened, incomplete or missed abortion, hydatidiform mole and chorionepithelioma) the ordinary hormone pregnancy test cannot be dispensed with for the time being.

7. The hyperæmia hormone pregnancy test in rats is based on the appearance of anterior pituitary reaction II, which is one of the decisive principles used in the ordinary hormone pregnancy test.

Intra-Arterial Injection of Penicillin for Infections of the Extremities

By S. T. GLASSER, *et al.*

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXVIII, 14th July, 1945, p. 796)

1. TWENTY-FOUR cases of severe infections of the extremities were successfully treated by the intra-arterial injection of penicillin.

2. The intra-arterial route allows for greater local concentration of penicillin.

3. Relief of pain is observed.

4. Amputation may be obviated in many cases.

5. Lower amputation sites are more frequently permissible.

6. Primary closure of the stump in the presence of infection is successful.

7. One injection may effect a cure in the presence of inflammation without suppuration of necrosis.

8. The method is economical and rapid in its effect.

Methylene Blue Test for Bilirubin in the Urine

By S. S. GELLIS, *et al.*

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXVIII, 14th July, 1945, p. 826)

AN aqueous solution of methylene blue (0.2 per cent based on actual dye content) is added drop by drop to 5 c.c. of urine and the total number of drops required to impart a blue colour to the urine-methylene blue mixture is noted. If more than 8 drops are required a smaller measured amount of urine is diluted to 5 c.c. and the test repeated in order that a clearer end point may be obtained. If diluted, the number of drops is multiplied by the dilution factor. The reading (in drops) is taken as one less than the number needed to change the colour from green to blue. A reading greater than 4 drops has been regarded as a positive test for bilirubin in the urine. Although the sensitivity of the test was diminished by the use of this criterion, its specificity was increased greatly, as indicated by the infrequent occurrence of falsely positive tests. Readings of 2 to 4 drops inclusive have been regarded as suggestive and as an indication for additional studies. As already stated, our investigations of this modified methylene blue test have been confined almost entirely to the study of urines from patients with infectious hepatitis. In this condition the modified test has yielded information of considerable value both in respect to early diagnosis and as a simple means of following the course of the disease. Furthermore, positive tests have been obtained with the urines from many hepatitis patients before the appearance of overt jaundice. An additional contribution of the test has been the roughly quantitative information it provides concerning changes in the excretion of bilirubin in the urine.

The methylene blue test, in our experience, has been inferior in sensitivity and specificity to the Harrison and diazo 'spot' tests for bilirubin in the urine. On the other hand, when positive, it provides better quantitative evidence concerning the output of urine bilirubin

than is afforded by the 'spot' tests and it can be performed under conditions which do not permit the use of the latter. For these reasons it is our opinion that the modified methylene blue test, properly used and interpreted, will prove to be a valuable procedure.

Prolonged Blood Concentrations After Oral Administration of Modified Penicillin

By H. WELCH, *et al.*

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXVIII, 21st July, 1945, p. 845)

A METHOD of oral administration of penicillin modified with either aluminium hydroxide or magnesium hydroxide results in prolonged blood concentrations of this drug.

Blood levels of from 0.03 to 0.19 unit per cubic centimetre may be obtained for as long as twenty-four hours after the administration of 100,000 units in four doses of 25,000 units each. In some persons, serum concentrations of 0.06 unit were obtained thirty hours after the administration of 100,000 units in four doses of 25,000 units each.

Following each dose there is a pronounced increase in the blood concentration level of penicillin, and this blood level may be increased with subsequent doses. Relatively high levels of penicillin may be maintained in blood by increasing the frequency of the doses of penicillin-aluminium hydroxide.

Since the modified penicillin may be prepared at the time of use, no stability problem is involved.

After oral administration of the modified penicillin, relatively small amounts are excreted in the urine. The penicillin is apparently largely inactivated within the body. It appears that some absorption through the stomach wall is obtained followed by further slow absorption from the small intestine.

Because of prolonged penicillin concentrations in the blood following this method of oral administration, this dosage form may have some prophylactic value.

Penicillin and Sulphonamides in the Therapy of Actinomycosis

By L. DOBSON
and
W. C. CUTTING

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXVIII, 21st July, 1945, p. 856)

1. SIXTEEN cases of actinomycosis were treated with sulphonamides or penicillin. These cases include 3 pulmonary, 2 abdominal and 11 of the cervicofacial types.

2. Of the 16 cases treated, 7 may be considered cured and 7 arrested, while 2 ended fatally.

3. *In vitro* tests corroborate the clinical impression of varying susceptibility of actinomyces of sulphadiazine and penicillin and of the slightly greater efficacy of sulphadiazine in certain instances.

4. The results in these cases indicate that both penicillin and the sulphonamides are highly effective drugs in the treatment of actinomycosis.

Determination of Hæmoglobin

By J. T. VAN BRUGGEN

(Abstracted from the *Journal of Laboratory and Clinical Medicine*, Vol. XXX, July 1945, p. 611)

1. BLOOD diluted 1 : 200 in 0.1 per cent carbonate, having a pH of 10.5, is unstable at elevated temperatures. Data are presented which indicate that the oxyhæmoglobin is probably converted first to methæmoglobin and later to hæmatin derivative.

2. If the pH of the solvent is lowered to approximately 8.0, the oxyhæmoglobin solutions are stable over a prolonged period.

Acute Infectious Hepatitis in the Mediterranean Theatre

By M. H. BARKER, *et al.*

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXVIII, 4th August, 1945, p. 997)

1. THE course of acute infectious hepatitis is usually characterized by an acute febrile non-icteric prodromal stage of one to two weeks' duration followed by the acute icteric stage. The convalescent stage is treated separately because of certain special features.

2. The condition of acute hepatitis without jaundice is a milder form of the icteric disease. This type of hepatitis, which is probably as common as that with jaundice, is important because inadequate treatment may result in the development of chronic hepatitis and also because of the epidemiologic implications.

3. The fundamental effect of exercise in producing relapse has led to the use of an exercise tolerance test for purposes of diagnosis and for the determination of the disease. exercise will result in an enlarged and tender liver which persists for several days or weeks.

4. Early and reasonably strict bed rest of adequate duration and a high protein diet are the fundamental therapeutic measures and will result in shortening the course of the disease and decreasing the incidence of chronic hepatitis. The disappearance of jaundice is not necessarily an indication of recovery.

5. The average case of infectious hepatitis requires from six to eight weeks for recovery. From 5 to 10 per cent are still not clinically well at the end of three months.

An Ætiologic Consideration of *Donovania Granulomatis* Cultivated from Granuloma Inguinale (Three Cases) in Embryonic Yolk

By K. ANDERSON, *et al.*

(Abstracted from the *Journal of Experimental Medicine*, Vol. LXXXI, January 1945, p. 25. As abstracted in the *Bulletin of Hygiene*, Vol. XX, June 1945, p. 321)

SINCE 1905, when Donovan first described the intracellular bodies now known to be fairly consistently present in smears from the ulcerated lesions of granuloma inguinale (commonly known in Britain as ulcerating granuloma of the pudenda), it has been presumed that these bodies, which were thought by Donovan to be protozoal in nature, were in fact the causative organisms of the disease. Up to the present, however, neither these bodies nor any other suspected ætiological agent has been isolated and cultivated outside the human body.

In a previous paper Anderson described the successful cultivation, on the yolk of living chick embryos, of micro-organisms indistinguishable from Donovan bodies. In this article the technique of their isolation and culture is described in considerable detail and it is particularly noteworthy that it has been found that these Donovan micro-organisms fail to grow on any ordinary artificial culture medium. Though the authors now consider the micro-organism to be a bacterium and not a protozoon, and to be the ætiological agent of granuloma inguinale, it has not so far proved to be pathogenic for common laboratory animals, including *Macacus rhesus* monkeys. Persons infected with the disease, however, are hypersensitive to injection into the skin of suspensions of the organism, and their sera give precipitin and complement-fixation tests with solutions of capsular substance. Inoculated chickens also give serological reactions of the same kind.

The authors propose the generic name *Donovania* to include the different strains of this organism, and for the specific type that of *Donovania granulomatus*.

Penicillin in the Treatment of Infantile Congenital Syphilis

By R. V. PLATOU, *et al.*

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXVII, 10th March, 1945, p. 582. As abstracted in the *Bulletin of Hygiene*, Vol. XX, July 1945, p. 399)

THIS is a preliminary note concerning 69 infants with manifest early congenital syphilis treated with penicillin in a total dosage of 16,000 to 32,000 Oxford units per kilo given as 60 intramuscular injections three-hourly over 7½ days. Thirty-nine of the infants have been followed for 4 to 12 months, with the results shown in the following table:—

	Cases	Percentage
Clinical results:		
Course uneventful ..	37	..
Clinical relapse ..	2	..
Serological results:		
Reversed to negative ..	21	54
Reversed to doubtful ..	4	10
Still positive but titre declining ..	9	23
Serological relapse ..	5	13

In the 69 cases there were 34 reactions, mostly mildly febrile. One infant had a severe collapse 48 hours after treatment was begun; three infants died 24 hours, 7 days and 9 days respectively after treatment was begun; all were in poor condition; two others died 5 and 14 weeks after penicillin.

Immediate response was generally good, lesions healing and spirochetes disappearing in much the same time as in the acquired disease; x-ray evidence of osteitis disappeared in 2 to 6 months, enlargement of liver, spleen and glands regressed in about three months and abnormal spinal fluid changes, where present, returned to normal in eight days to six months.

It is concluded that the total dose should be increased to 40,000 O.U. per kilo, that relapse should be treated with double this dose and that adequate supportive care of acutely ill infants is a vital necessity.

(Nothing is said about the possible danger of Herxheimer reactions in cases with extensive lesions; it might be well, in such, to give smaller doses during the first few days.)

Promin in Pulmonary Tuberculosis

By R. J. DANCEY, *et al.*

(Abstracted from the *American Review of Tuberculosis*, Vol. XLIX, June 1944, p. 510. As abstracted in the *Bulletin of Hygiene*, Vol. XX, June 1945, p. 310)

A SERIES of 27 cases of pulmonary tuberculosis was treated with promin, of whom five were excluded from analysis because of insufficient treatment, and six because of concurrent collapse therapy. Individual case notes are given for the remaining 16.

The drug was given by mouth, usually in 0.4 gm. capsules, after meals. Treatment started at 0.4 gm. daily, and increased by 0.4 gm. every tenth day, until the usual maintenance level of 1.2 gm. daily was reached. Three patients received 2.0 to 2.4 gm. daily. Treatment was continued for 1 to 12 months, median five and one-half. 'Not infrequent' rest periods of five to seven days were interposed because of toxic reactions.

The median dosage value, including rest periods, for the sixteen cases was 1.07 gm. daily.

In four cases the drug was given intravenously, or intramuscularly, in doses of 5 gm. and 2 gm., respectively, in 40 per cent solution.

At the usual daily dosage of 1.2 gm., blood levels taken before the morning dose, were 4 to 6 mg. per 100 c.c., once below 3 mg. and twice above 8 mg. The three patients receiving 2.0 to 2.4 gm. daily showed levels of 12, 6, and 6 mg., respectively. Those treated parenterally showed 2 to 3 mg. 12 to 18 hours after the last dose.

With oral dosage of 0.5 to 1.2 gm., urine levels were 60 to 140 mg. per 100 c.c., and 24-hour excretion of colour producing compounds, calculated as promin, was greater than the promin intake in every case but one, the excess reaching 130 per cent. Maresh is cited as observing that promin solutions gave stronger colour reactions after treatment with fresh human pancreas, and the authors suggest a possible liberation in the bowel of the parent diaminodiphenylsulphone which, in blood or urine, gives stronger colour reactions than promin at equivalent molecular concentrations.

In one case of tuberculous meningitis the promin level in the spinal fluid was higher than the blood level on two occasions—4 mg. and 17 mg. against 2 mg. and 12 mg.

The Effects of Concentrated Hyperimmune Rabbit Serum in Louse Borne Typhus

By A. YEOMANS

J. C. SNYDER

and

A. G. GILLIAM

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXIX, 1st September, 1945, p. 19)

TWENTY-FIVE patients with louse borne typhus were treated with refined and concentrated hyperimmune antityphus rabbit serum. Their clinical course was contrasted with that of 44 'untreated' cases.

The 10 patients who received serum in the first seventy-two hours of illness had mild uncomplicated typhus of short duration.

The 15 patients who had been sick for four, five or six days before serum was administered did not show a striking difference in clinical severity from the 'untreated' controls, except that there were no fatal cases.

It is concluded that hyperimmune antityphus rabbit serum has a favourable therapeutic effect on the course of typhus if treatment is started in the first three days of the disease. Although serum treatment seemed to have reduced the mortality in the group of patients who received serum in the fourth, fifth and sixth days of illness, the value of serum therapy for late cases cannot be determined definitely from the data of this study.

Reviews

AN INDEX OF DIFFERENTIAL DIAGNOSIS OF MAIN SYMPTOMS.—By various writers. Edited by Herbert French, C.V.O., C.B.E., M.A., M.D. (Oxon.), F.R.C.P., and A. H. Douthwaite, M.D., F.R.C.P. Sixth Edition. 1945. John Wright and Sons, Ltd., Bristol. Pp. viii plus 1128, with 798 illustrations of which 231 are coloured. Price, £4 4s.

It is good that it has been possible to bring out a new edition in spite of war-time difficulties. Dr. Arthur H. Douthwaite has assisted the veteran editor in its

preparation. The scope of the work remains as when the book was first published in 1912, *viz.* establishment of diagnosis by differentiating between the various diseases to which a particular symptom may be due. The arrangement is in alphabetical order, and the general index which covers over 180 pages, further facilitates references. However experienced a doctor may be, there will always be need for a reference book like this in his library.

R. N. C.

SICK CHILDREN: DIAGNOSIS AND TREATMENT: A MANUAL FOR STUDENTS AND PRACTITIONERS.—By Donald Paterson, B.A. (Manitoba), M.D. (Edin.), F.R.C.P. (Lond.). Fifth Edition. 1944. Cassell and Company, Limited, London. Pp. viii plus 440, with 23 half-tone plates and 84 figures in the text. Price, 16s.

This is the fifth edition since this book first appeared in 1930. This edition has come out with considerable revision of a number of sections in the text, incorporating the recent advances made in paediatrics. The additional subjects include the use of penicillin, modern views on hæmorrhagic diseases of the new-born and erythroblastosis foetalis and vitamin requirements of infants and children. The book is well proportioned, well illustrated and readable, and a large amount of information is given in a very compact volume. The descriptions, though concise, are fairly adequate, the main stress having been laid, as the title suggests, on diagnosis and treatment, thus making the book practical. The manual ends with a small chapter on intestinal parasites that are commonly found in childhood in the British Isles; this is followed by an useful appendix. The book makes no special mention of diseases of children in the tropics. Perhaps this is too much to expect.

R. N. C.

TEXTBOOK OF ANÆSTHETICS.—By R. J. Minnitt, M.D. (Liverpool), D.A., R.C.P. & S. (Eng.), and John Gillies, M.C., M.B., Ch.B. (Edin.), D.A., R.C.P. & S. (Eng.). Sixth Edition. 1944. E. and S. Livingstone Limited, Edinburgh. Pp. viii plus 487. Illustrated. Price, 25s. Postage, 9d. (home)

THE book covers the whole range of anæsthesia from the simplest 'open ether' to the more specialized branches such as cyclopropane, spinals and splanchnics. After some necessary theoretical considerations and a description of the phenomenon of anæsthesia, the authors proceed to discuss the pre-operative preparation of the patient, premedication and basal narcosis. A chapter is devoted to the various postures which are requisite for the performance of particular types of operation. Various forms of inhalational anæsthesia are then described; then intravenous anæsthesia in dentistry and obstetrics. The accidents and sequelæ of anæsthesia are dealt with from a practical point of view. The subject of shock receives special attention; the authors consider low spinal block justifiable for operation below the level of the umbilicus, where the degree of shock is moderate and the blood pressure is above 100 mm. Hg. Recent findings on the dangers of trichlorethylene in a closed circuit and of pentothal injected accidentally into the arteries are given. There is a long but very useful chapter on the choice of anæsthetics according to the patient's age, sex and habits, the anæsthetist's ability, types of operation and the presence of concurrent pathological lesions such as diabetes, heart and liver disease. The last chapter is on local and regional anæsthesia, and one wishes it had been given more space, but, as the authors say, 'it is beyond the scope of this book'.

The book bears the marks of the authors' practical and teaching experience. It is comprehensive and up to date, with a lucid text and many useful drawings and photographs. It is well-produced—the paper is

good and the type is clear. The novice and the specialist will both derive benefit from it.

R. N. C.

MIDWIFERY FOR NURSES.—By Aleck W. Bourne, M.A., M.B., B.Ch. (Camb.), F.R.C.S. (Eng.), F.R.C.O.G. Third Edition. 1944. J. and A. Churchill Limited, London. Pp. viii plus 296, with 111 illustrations. Price, 7s. 6d.

In the preface to the third edition of this book, Bourne writes 'Nutrition of the mother both before and after labour which will ensure quality rather than quantity of food, exercises during the antenatal period, and a quiet mind throughout pregnancy are all factors for normal childbearing which must absorb more and more of the midwife's attention'. This is excellent since these are the fields in which the midwife's influence can be most beneficially exerted. It is therefore rather unfortunate that paper restrictions have limited the space which could be given in this edition to developing these aspects of prenatal care and to stressing the rôle of the midwife as a health educator, not merely as the agent who brings the mother under medical supervision for the prevention, detection, and treatment of abnormalities.

In the chapter on infant feeding, complicated directions are given for artificial feeding while nothing is said about consulting a doctor before resorting to this method. Feeding by the clock may be unnecessary in a busy hospital but the desirability of studying the nursing couple and allowing latitude under more favourable conditions might be mentioned.

These comments deal with refinements in the training of midwives, the basic knowledge required by the midwife is clearly and concisely set out. The book is excellently illustrated and the field covered includes sections on anatomy, physiology, and bacteriology sufficient to enable the midwife to practise her profession intelligently and successfully.

Mr. Bourne's long connection with the training and examination of midwives and his outstanding position as an obstetrician are sufficient guarantee that the book gives a sound comprehensive and practical presentation of the subject.

J. M. O.

MODERN TREATMENT YEAR-BOOK, 1945: A YEAR-BOOK OF DIAGNOSIS AND TREATMENT FOR THE GENERAL PRACTITIONER.—Edited by Cecil P. G. Wakeley, C.B., D.Sc., F.R.C.S., F.R.S.E., F.A.C.S., F.R.A.C.S. (Hon.). Published by The Medical Press and Circular, London. Pp. viii plus 296. Illustrated. Price, 15s.

THIS volume contains forty-five selected articles on medicine and surgery, and ranges over a variety of subjects from neurosis to fracture of the spine. Written in a practical manner, they give the modern diagnostic methods and the new types and forms of treatment. Many of the articles will be useful to the general practitioner.

R. N. C.

THE ANALYSIS AND INTERPRETATION OF SYMPTOMS.—Edited by Cyril M. MacBryde, M.D. 1944. Published by J. B. Lippincott Company, Philadelphia and London. Pp. v plus 302. Illustrated

THERE is, at the present time, a tendency to over-stress the importance of various mechanical measures and laboratory methods in the diagnosis of diseases. The symptoms provide really the most important data in the diagnosis of cases and all signs and laboratory data have to be evaluated only in the light of these symptoms.

The book under review is intended to help in the understanding of the significance of the symptoms and in their differential diagnosis. The different chapters are devoted to: Nervousness and fatigue, fever, headache, thoracic pain, cough and hæmoptysis, abdominal

pain, hæmatemesis and melæna, jaundice, joint pain, and obesity, and these are quite common symptoms for which the patient comes to his physician.

The chapters are well written and will be of help to the students and the practitioners in understanding the mechanism of the production of symptoms and in the diagnosis of the underlying diseases causing them.

P. C. S. G.

A HANDBOOK OF PSYCHOLOGICAL MEDICINE. (WITH A CHAPTER ON WAR-TIME MENTAL DISORDERS.)—By Ajit K. Deb, M.Sc., M.B. (Cal.), D.P.M. (Lond.). 1945. Published by U. N. Dhur and Sons Limited, Calcutta. Pp. viii plus 194. Price, Rs. 5

THIS little book, meant for practitioners and medical students, describes the essentials of mental disorders and their treatment. The book is not burdened with technicalities and contains much useful information.

The introduction which occupies only one page might have been expanded to give an exposition of the principles of psychological medicine. The chapters on signs, symptoms and causes of mental diseases are comprehensive, but some of the explanations and descriptions might appear a little difficult especially to the beginner. Then follow descriptions of various forms of psychosis and psychoneurosis, including mental disturbances in childhood. An outline is given of the different forms of psychotherapy, and some physical methods of treatment are described. At the end there is an informative chapter on the legal aspects of mental disease. We hope that the author may be able to include in a future edition some illustrative cases of minor mental disorders which are nowadays too common, but of which the nature is often missed by inexperienced doctors.

R. N. C.

PSYCHOLOGY AND PSYCHOTHERAPY.—By William Brown. Fifth Edition. 1944. Edward Arnold and Company, London. Pp. vii plus 223. Price, 14s.

ONE of the two new chapters added in this edition is on the psychology of modern Germany; this with the chapter on psychology of peace and war gives a reasoned view of the origin of the war from psychological point of view. According to the author, it is the paranoid tendency of mind that is primarily responsible, in modern civilized society, for so much fanatical conflict in the world. After the defeat of 1918, Germany passed through a phase of deep depression, and this was followed by outbursts of collective self-assertion with denial of military defeat; scapegoats were created in the form of Jews, Freemasons and Bolsheviks. Hitler rose to power and was acclaimed as leader. The hysterical and paranoid tendencies that were a feature of his character had their counterpart in the reaction of the entire nation and led to maniacal attacks on the neighbouring states. The author believes that a certain amount of analysis would benefit the leaders of nations; they would be made aware of the mental forces at work below the surface.

The book has been thoroughly revised and presents the subject-matter in a wise and rational manner. It should appeal to both doctors and laymen seeking to know the working of the mind.

R. N. C.

FOOD FAMINE AND NUTRITIONAL DISEASES IN TRAVANCORE (1943-44).—By K. G. Sivaswamy and others. Servindia Kerala Relief Centre, Coimbatore. 1945. Pp. 265, with 33 illustrations. Price, Rs. 5

THIS report consists of many sections. Some sections deal with surveys of special areas, with studies of population, deaths in general, deaths caused by starvation, the incidence of disease, social and economic conditions, rationing, housing, sanitation, water supply,

income, indebtedness, and so on. Special sections deal with disease caused by malnutrition, some with the attendance of patients at a hospital; some report nutritional surveys of special areas with notes on family diet, food values, etc. One section discusses vital statistics and public health. The death rate in 1942-43 was the highest in the last decade, and in 1943-44 it was even higher. Registered deaths showed a marked rise and estimated deaths were considered to be much higher.

The causes of the famine are discussed and the different diseases causing death are described. The report is a valuable and interesting one, but some of the medical information is not very accurate or informative.

BOOKS RECEIVED

1. The treatment of acute intestinal obstruction. By Judson T. Chesterman. Published by J. and A. Churchill Limited, London. Pp. viii plus 116, with 13 illustrations. Price, 10s. 6d.

2. The venereal diseases: A manual for practitioners and students. By James Marshall. Published by Macmillan and Company, Limited, London. Pp. xi plus 348. Illustrated. Price, 21s.

3. A history of comparative anatomy. (From Aristotle to the eighteenth century.) By F. J. Cole. Published by Macmillan and Company, Limited, London. Pp. 524. Illustrated. Price, 30s.

4. Adhunik Netra-Rog Bignan Shastra. (Ophthalmology.) Written in Hindi. Volume I. Part I. By D. D. Sathye. Published by the author (39, Poddar Road, Cumbala Hill, Bombay-26). Illustrated.

5. The cookery book for diabetics. Compiled by The Diabetic Association, London (9, Manchester Square, W.1). Published by H. K. Lewis and Company Limited, London. Pp. 74. Illustrated. Price in Great Britain is 4s.

6. A handbook on diseases of children including dietetics and the common fevers. By Bruce Williamson. Fourth edition. Published by E. and S. Livingstone Limited, Edinburgh. Pp. xii plus 388. Illustrated. Price, 12s. 6d. Postage 6d. (home).

7. A practice of orthopaedic surgery. By T. P. McMurray. Second edition. 1945. Published by Edward Arnold and Company, London. Pp. viii plus 435. Illustrated. Price, 30s.

8. Penicillin therapy. By J. R. Goyal. Printed and published by B. Datta, Esqr., Manager, The Albion Press, Kashmir Gate, Delhi. Pp. 148. Price, Rs. 5. Available from *The Medical Review of Reviews*, Burn Bastion Road, P. O. Box No. 160, Delhi.

9. Radium therapy: Its physical aspects. By C. W. Wilson. Published by Chapman and Hall Limited, London. Pp. xi plus 224. Illustrated. Price, 18s.

10. A textbook of pathology: General and special for the use of students and practitioners. By J. Martin Beattie and W. E. C. Dickson. Fourth edition. Published by William Heinemann Medical Books Limited, London. Pp. xiv plus 1368, with over 800 illustrations in the text and 19 coloured plates from original preparations. Price, 84s.

11. Outlines of physical methods in medicine. By G. D. Kersley. Published by William Heinemann Medical Books Limited, London. Pp. ix plus 85. Illustrated. Price, 6s.

12. Physical treatment by movement, manipulation and massage. By James B. Mennell. Fifth edition. Published by J. and A. Churchill Limited, London. Pp. xi plus 512, with 288 illustrations, some in colour. Price, 30s.

13. Recent advances in obstetrics and gynaecology. By A. W. Bourne and L. H. Williams. Sixth edition. Published by J. and A. Churchill Limited, London. Pp. x plus 357, with 77 illustrations. Price, 18s.

14. The Exodus from Travancore to Malabar Jungles. Surveys by Shri K. G. Sivaswamy, Lt.-Col. T. S. Shastri, Dr. T. D. Nair, Dr. T. S. Nair, Dr. P. A. Narayanan, Dr. C. V. Narayana Aiyar and

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- Dr. Miss Atzorri. Published by Servindia Kerala Relief Centre, R. S. Puram Post, Coimbatore, S. India. Pp. 39 plus iv. Price, Re. 1.
15. Extensile exposure applied to limb surgery. By Arnold K. Henry. Published by E. and S. Livingstone Limited, Edinburgh. Pp. viii plus 180. Illustrated. Price, 30s. Postage, 7d. (home).
16. The rheumatic diseases. By G. D. Kersley. Second edition. Published by William Heinemann Medical Books, Limited, London. Pp. xii plus 120. Illustrated. Price, 15s.
17. The medical annual: A year-book of treatment and practitioner's index. Edited by Sir Henry Tiddy and A. Rendle Short. Sixty-third year 1945. Published by John Wright and Sons Limited, Bristol. Pp. lxxviii plus 410. Illustrated. Price, 25s.

Abstracts from Reports

ANNUAL REPORT ON THE HEALTH OF THE ARMY IN INDIA IN 1943

The health of the army in 1943, while not so good as in previous years, showed considerable improvement over 1942; and taking into account the many adverse factors which were present through the year, may be considered as having been satisfactory.

The year was one of great difficulty for India. There was a war on her frontier 'in the most unhealthy region in the world'; the presence of civilian labour all over India in close proximity to troops was ever a source of infection, and the formation of camps for training in malarious regions was one of the most potent factors in producing malaria. In the case of Indian troops there were the additional factors such as overcrowding, inadequacy of rations, and the poor state of health of the recruits on enlistment, many of whom were suffering from anaemia and malnutrition. On the other hand, there was no malaria epidemic among the civil population as in 1942, the sanitary discipline improved, and the majority of British troops became acclimatized.

Malaria was the most prevalent disease, and admissions from this cause were very high indeed. There was a marked decrease in sandfly fever and oriental sore due, in part at least, to the intensive anti-mosquito spraying to which the sandfly is more vulnerable than the mosquito. The extremely low incidence of the enteric group of fevers was maintained, a testimony to the efficacy of protective inoculation. On the other hand, the diarrhoea-dysentery group, although substantially decreased, was still at about double the average pre-war rate. These diseases were most common in June, July and August. The protozoal type was twice as common among the British as with the Indian troops, but the bacillary type predominated in both. Except for one outbreak, cholera was rare—a remarkable tribute to the army sanitary measures. Routine inoculation is not practised nowadays; it is only done when there is serious outbreak in a civil population in close proximity to troops. The low incidence of smallpox during the year is considered too high for military personnel, as it is an easily preventable disease. It occurred among those who had not been successfully vaccinated or re-vaccinated. In spite of the strains and stresses of wartime, there was no increase in tuberculosis. The incidence of venereal disease continued to be high. Compared to 1942, there was marked decrease in the admissions for heat-stroke and heat-exhaustion, but the rate was still about double that of the average of pre-war years. There was an enormous increase in scabies.

23.3 per cent of Indians that came for enlistment were rejected, the principal causes being venereal diseases, diseases of heart, malaria, defective vision, trachoma, anaemia and skin diseases.

Eastern Army (including 14th Army).—The army was located and had to fight in regions which are regarded

as the most malarious in the world. Naturally malaria was unduly prevalent. Dysentery and diarrhoea were also very common. The rates for venereal diseases were much higher than in the rest of India, the explanation being that troops returning after months of extreme hardship in the forward areas fell an easy prey to the prostitutes who infested the towns and cities.

The last section of the report deals with developments in anti-malaria measures, and with the food and nutritional problems which were complicated by factors such as food shortage, jungle warfare, etc. In view of the difficulties that had to be faced, the army authorities might well be proud of their achievements during a critical period of the war.

THE ROSS INSTITUTE OF TROPICAL HYGIENE, INDIA BRANCH: REPORT OF THE COMMITTEE OF CONTROL FOR THE COMPLETED 31ST JULY, 1945

At the annual meeting held in August Mr. Bannerman referred to the assistance given to the military authorities by the Indian Tea Association, the biggest supporters of the Institute, and presented its report for the year ending July 1945.

The war on the north-east frontier of India, the report says, has markedly affected public health conditions in Assam and Bengal. Not only has there been much increase in sickness, lowered birth and increased death rates, but hitherto uncommon diseases and new strains of organisms have been introduced, apparently due to importation of refugees from Burma and of troops and labourers from other provinces and foreign countries. Diseases such as louse-borne typhus and relapsing fever have never previously been recorded in Assam tea estates. Filariasis previously limited to a few areas is now occurring everywhere. Venereal diseases have become an important problem and tertiary malaria predominated to the extent of about 75 per cent, a change over has taken place with the benign tertiary parasite now representing over 50 per cent new infections. Labourers who had previously been immune to local malaria now develop severe attacks—this may be due to introduction of new strains of parasites from Africa and other countries.

Reference is made in the report to Iyengar's views on water hyacinth and malaria, which, if confirmed, will be an important advance in the prevention of malaria. Much money and energy have been spent in the past to eradicate this aquatic plant as an anti-malaria measure. For lack of supplies, only limited experiments were possible with DDT. Its use, however, needs caution, as it may kill fish and other forms of aquatic life. The prevention of malaria by cheap biological measures such as flushing streams and shading drains with vegetation continues to progress and give good results in estates.

At the Labac Central Hospital (Assam) and in the subsidiary estate hospitals isolation wards are provided for tuberculous cases. A colony has been founded which cares for 30 lepers. During a visit to Jaipur Estate Dr. Ramsay noticed a high incidence of 'Nagasaki'.

Many laboratory technicians and field workers in malaria have been trained. Many doctors, technicians and surveyors conversant with malaria problems have been supplied to the army since the beginning of the war.

THE ANNUAL REPORT OF THE MISSIONARY MEDICAL COLLEGE FOR WOMEN AND HOSPITAL, VELLORE, FOR THE YEAR 1944-45

It is stated in the report that there has been a rapid development of the college, and it is expected to be soon recognized as an M.B., B.S. college. During the

year teaching and hospital work were continued satisfactorily; several new members joined the senior staff, but still more are needed as heads of other departments. A donation of a lakh of rupees has been received for building up a mental and nervous diseases hospital. The future plan of Vellore is to start co-education and develop special units, viz, rural medical unit, tuberculosis unit, etc., in addition to the main pre-clinical and clinical departments. There is also a plan to start a University School of Nursing.

Correspondence

CÆSAREAN SECTION

SIR,—In regard to the contribution of mine on 'Cæsarean Section' published by you in August 1945, I should like to amplify one point which may help to obviate the disappointment of some novice when using the abdominal nerve block.

It is always easy to block the thoracic nerves but the ilio-inguinal and ilio-hypogastrics are often difficult. Bishop, Carr, Anson and Ashley (Quarterly Bulletin, Northwestern University Medical School, Chicago, 1943 Fall Quarter), have demonstrated the great frequency of distal anastomoses between the nerves to the anterior abdominal wall.

I have bilaterally dissected the thoracic XII, ilio hypogastric and ilio-inguinal nerves on four unpreserved subjects within 24 hours of death. In every instance the nerves had a different pattern and position, even on the two sides of the same subject.

From the above and from practical experience I conclude that to be certain of blocking the ilio-hypogastric and ilio-inguinal nerves it is necessary to infiltrate the internal oblique muscle from 3 to 4 cm. cephalad to 2 cm. caudad to the anterior superior iliac spine in a line 2 cm. medial to the spine, and that the infiltration must be continued laterally and cephalad through the internal oblique and transversalis muscle to a distance of 3 to 4 cm. from 3 to 4 cm. cephalad to 2 to 3 cm. caudad to the iliac crest. Such an infiltration requires 20 c.c. 1 in 200 novocaine (procaine), 1 in 2,000 nupercaine or 1 in 3,000 amethocaine in 0.9 per cent saline solution.

When the correct technique has been acquired the results will be found satisfactory. Speed comes with practice.

F. R. W. K. ALLEN.

INDIAN MILITARY HOSPITAL,
POONA,
3rd October, 1945.

THE IMMEDIATE NEED OF REFORM OF THE MEDICAL COUNCILS OF INDIA

SIR,—I have read the communication of Dr. R. S. Greval in the May 1945 issue of your esteemed journal (pp. 281-2). While I am very much with the writer as regards the necessity of reforms in our Councils, I wish to point out that the medical act of England of 1858 was passed and the General Medical Council set up which registered all persons who were practising medicine at that time including so-called quacks, and not only qualified medical men, as the writer mentions. Nor is the main function of the General Medical Council 'to register medical students', etc. This is entirely wrong. It has no such function at all.

U. B. NARAYAN RAO.

1, DAMODAR MANSIONS,
OPERA HOUSE, TRAM TERMINUS,
BOMBAY 4,
4th October, 1945.

TROPICAL EOSINOPHILIA

SIR,—In a fairly large number of cases of tropical eosinophilia treated by me, the differential count has revealed a very high increase in lymphocytes. Immature forms are common. An association of these with eosinophilia would seem to augur a dramatic response to arsenical therapy. The eosinophilia, though occasionally reaching very high figures, is not so constantly marked as this lymphocytosis. So that I think that the term eosinophilia now applied to the blood picture is incomplete as well as misleading.

T. BALAKRISHNAN, M.B., B.S.

ASOKA HOSPITAL,
CALICUT,
7th November, 1945.

[Note.—We have observed a lymphocytosis in about one-third of our cases only during the course of arsenical treatment, being most marked in a patient developing agranulocytic angina (*vide Indian Medical Gazette*, March 1945, p. 151). The lymphocytes appeared to be morphologically normal.—EDITOR, I.M.G.]

CONGENITAL ABSENCE OF THE SHAFT OF THE FEMUR ON BOTH SIDES

SIR,—The case reported by Capt. Katdare in the June number of the *Indian Medical Gazette* (Congenital Absence of the Shaft of the Femur on Both Sides) is extremely interesting. In view of the rarity of the condition, it is rather depressing to read, 'The family history is of no importance'. Writers on heredity like Gates (1929), Baur, Fischer and Lenz (1931), and Snyder (1941), all agree that absence of the patella is a hereditary condition determined by a dominant gene. One should therefore expect one of the parents to show this condition.

Again, the left hand appears to be a variety of split-hand or lobster-claw (I hope the writer means this when he calls it a typical 'claw-hand'), which also is determined by a dominant gene. According to genetic principles, one of the parents should show this deformity also. Even assuming that the condition is recessive as Lenz believes, it would be worth while to find out if the parents in this case were cousins or not.

It is not my intention to suggest that Capt. Katdare has neglected the family history; I only suggest an enquiry in greater detail.

K. A. SHAH.

RANCHHODLAL DISPENSARY,
AHMEDABAD,
12th November, 1945.

REFERENCES

- BAUR, E., FISCHER, E., *Human Heredity*. George and Lenz, F. (1931). Allen and Unwin Ltd., London.
GATES, R. R. (1929) .. *Heredity in Man*. Constable and Co., Ltd.; London.
SNYDER, L. H. (1941) .. *Medical Genetics*. Duke University Press, Durham.

Service Notes

APPOINTMENTS AND TRANSFERS

THE Central Government is pleased to nominate Colonel S. L. Bhatia, M.C., Inspector-General of Civil Hospitals, Assam, to be a member of the Medical Council of India from Assam, with effect from the 30th August, 1945, vice Colonel W. E. R. Dimond, C.I.E., O.B.E., resigned.

The Central Government is pleased to nominate Lieutenant-Colonel G. R. McRobert, C.I.E., Inspector-General of Civil Hospitals, Bihar, Patna, to be a member of the Medical Council of India from Bihar, with effect from 9th June, 1945, *vice* Colonel W. C. Spackman, resigned.

Lieutenant-Colonel E. T. N. Taylor, C.I.E., is appointed as Additional Deputy Director-General, Indian Medical Service (Personnel), with effect from the afternoon of the 30th June, 1945.

Major J. Guthrie, Additional Civil Surgeon, Tibet and Bhutan, assumed charge of the post of Civil Surgeon, Tibet and Bhutan, on the forenoon of the 1st June, 1945.

Captain G. H. F. Humphreys is appointed to officiate as Agency Surgeon, Gilgit, with effect from the afternoon of the 6th July, 1945, and until further orders.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

To be Captain

Beni Madhab Basak. Dated 17th June, 1945.

To be Lieutenants

Krishnarao Seetaram. Dated 16th May, 1945.

15th June, 1945

Avinash Chandra Chopra. Shafique Yunus Siddique.

The undermentioned officers of the Indian Medical Service (Emergency Commission) revert from Indian Army Medical Corps and are seconded for service with the Royal Indian Navy Volunteer Reserve :—

6th June, 1945

Lieutenant Gul Hasan Pirzada.

Lieutenant D. A. W. Nugent.

Lieutenant R. Tyagarajan.

Lieutenant J. T. Marshall. Dated 5th June, 1945.

Lieutenant Mahindra Singh. Dated 25th June, 1945.

INDIAN MEDICAL SERVICE SECONDED TO THE INDIAN ARMY MEDICAL CORPS (Emergency Commission)

(WOMEN'S BRANCH)

To be Captain

Elizabeth K. Markos. Dated 14th April, 1945.

PROMOTIONS

Colonel to be Major-General

W. R. Stewart, C.B., C.I.E. Dated 12th July, 1945.

Lieutenant-Colonels to be Colonels

Lieutenant-Colonel S. L. Bhatia, M.C. Dated 11th June, 1945.

J. R. Kochhar. Dated 20th June, 1945.

S. M. A. Faruki. Dated 12th July, 1945.

Captain to be Major

K. N. Rao. Dated 1st July, 1945.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE SECONDED TO THE INDIAN ARMY MEDICAL CORPS (Emergency Commissions)

Captains to be Majors

T. Singh. Dated 2nd July, 1945.

V. K. Row. Dated 5th July, 1945.

H. Flack. Dated 6th July, 1945.

G. V. S. Murthi. Dated 16th July, 1945.

R. M. Nadkarni. Dated 17th July, 1945.

Lieutenants to be Captains

5th July, 1945

S. P. Jha.

M. A. Khan.

M. Sauaib.

S. A. R. Peerzada.

M. B. Azami.

R. K. Gupta.

N. H. Khan.

A. K. Mallik. Dated 6th July, 1945.

7th July, 1945

B. P. Gupta.

Y. D. Rishi.

C. M. Yasin.

V. P. Sharma.

K. Zaffar-ul-Aziz.

O. P. Modhok.

K. S. Rai.

O. P. Kapur.

S. M. A. Bokhari.

O. P. Chhabra.

C. M. Akram.

10th July, 1945

S. L. Chadha.

A. U. Khan.

E. A. Sinclair.

S. A. Syed.

A. R. Shaikh. Dated 11th July, 1945.

P. V. Rao. Dated 18th July, 1945.

M. S. Khera. Dated 21st July, 1945.

R. H. Baker. Dated 25th July, 1945.

RETIREMENTS

Major-General J. S. S. Martin. Dated 6th March, 1945.

Major-General H. J. M. Cursetjee, C.S.I., D.S.O., K.H.S. Dated 12th July, 1945.

Lieutenant-Colonel H. J. Rice, C.I.E., M.C., on account of ill health, 24th February, 1945, and is granted the honorary rank of Colonel.

RELINQUISHMENT

INDIAN MEDICAL SERVICE

(Emergency Commission)

Major A. D. Dyson, on account of ill health, 12th March, 1945, and is granted the honorary rank of Major.

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Original Articles

SOME OBSERVATIONS ON THE SURGERY OF THE HAND

By FRANKLYN V. STONHAM

LIEUTENANT-COLONEL, I.M.S.

Officer in charge of the Surgical Division of a General Hospital

Septic infections

PROBABLY the bulk of the more minor surgical work done in any military hospital consists of treating septic diseases of the fingers. Familiarity is apt to breed contempt, and the fact that a neglected whitlow may cause as much economic disability to the patient as a fractured spine is not always fully realized. The wastage of man-power is very considerable, and, as Denness (1944) puts it, a man may be off duty longer with a whitlow than after appendicectomy. Bad end-results and avoidable complications are still seen with regrettable frequency. Instructions have been issued discouraging perfunctory incision in medical inspection rooms, and orders have been given that septic diseases of the hand must be admitted at once to hospital, so that treatment can be supervised by a surgical specialist. Prompt admission to hospital is not always practicable, and soldiers do not always apply at once for treatment. In one hospital we investigated two hundred cases, and found that the time lag between the onset of infection and arrival at hospital averaged six days.

In some cases, infection occurs from abrasions, pricks with thorns, needles, etc., but a considerable number of patients state that infection has followed minor contusions from knocks, for instance, while working on an engine. Malnutrition probably plays some part, as septic infections of the hands seem to be more common in troops who have had only limited amounts of fresh food. Incision under general anaesthesia must be carried out at once. Chemotherapy and penicillin are useful aids to surgery, but attempts to abort infection are only justifiable when the case is seen very early. The practice of nicking an abscess without anaesthesia and squeezing out pus cannot be too strongly condemned. Neither should fomentations be used before the abscess has been opened. They may be useful when discharge is profuse, but should be discontinued as soon as the wound is reasonably clean, since they are likely to cause maceration of the tissues and delay in healing. Most cases clear up quickly with a plain vaseline dressing which need not be frequently changed, or an alcohol compress. Continued discharge should arouse the suspicion that the incision is inadequate, or that bone or tendon sheath infection has occurred.

The standard surgical textbooks do not give a great deal of help in the problem of the neglected case, a condition which is still unfortunately common.

In the case of the grossly swollen finger in which infection has been present for some days, the abscess must be completely laid open. This is carried out by a generous incision. The limits of the abscess are then determined by probing with the point of a Mayo scissors and cutting it open to the full extent, avoiding digital nerves. The incision is then packed open. The common practice of making a small incision on either side of the finger and pulling a piece of corrugated rubber drain through is unsound, and generally demands a larger incision later to allow escape of a sloughed tendon. The loss of the flexor tendon usually calls for amputation, and the sooner it is carried out the better.

Wounds

The aim should be to secure primary healing wherever possible, but this, of course, demands that the case must be seen early. The blood supply of the hand is excellent, and, after cleaning the skin and washing out the wound, only soiled tags and hopelessly damaged tissue should be removed.

Skin edges should never be excised as a routine, since it is not only unnecessary but prevents the wound from being closed without tension. Severe pulping of the muscles is not incompatible with primary healing, even when soiling and compound fractures of the bones are present, and fingers almost cut off but attached by a small pedicle of soft tissue with intact flexor tendons can sometimes be sutured into position and saved. We have had several successes in what looked almost hopeless cases even before the days of penicillin and sulphonamide. In some instances where the wound is seen late and infection seems probable, the choice lies between packing the wound open as a preliminary to secondary suture, and primary suture with local penicillin instillations in the hope of preventing suppuration.

Destructive injuries and wounds, especially those with established infection, are a very different problem. 'Save all you can' is a piece of advice which has religiously been copied from textbook to textbook, and its over-zealous application has not only led to much avoidable residual disability, but it has caused a great deal of unnecessary suffering. While it is true that many hands have been maimed by rash radicalism, conversely, many bad results have been due to unsound and indiscriminating conservatism. This was given emphasis by Oldham (1941), Crouch (1941), and the writer (1942). It is not tissue which is to be saved, it is function. Experience with war wounds has provided many examples which illustrate the futility of attempting to save fingers in which the injury has been of such a nature that restoration of function could not have been hoped for. Efforts to save

[Dec., 1945]

tissue which from the outset has been functionally destroyed jeopardize the entire limb. Many cases have been seen in which the hand has become stiff, probably permanently, following injury to one finger only, but even worse is to be feared, since some of these cases with chronic sepsis have eventually required amputation through the forearm, while others have developed psychoneurotic symptoms. There is no more grateful patient than one who, after many weeks or months of suffering, has been relieved of a useless and painful finger by a well-planned amputation followed by a good cosmetic result.

If the remaining fingers have become stiff or weak from pain, from the presence of adjacent infection, or from splinting, they soon show signs of improvement after the removal of the offending painful or stiff digit has permitted. By no means should all injured fingers and hands be submitted to drastic amputations when first seen, but the question of the justifiability of saving grossly damaged tissue, especially when infection is present or probable, needs very carefully to be weighed, and the following principles should be considered in arriving at a decision as to whether or not to amputate, and at what level.

1. Scars should if possible be dorsal. Scars on the palmar aspect are less desirable, while terminal scars should be avoided altogether. The tissue over the end of the finger should be reasonably loose over bone; otherwise retraction will cause stretching of the scar and chronic pain. Flaps should be fairly generous. In some cases, pedicle flaps can be used with advantage to graft uncovered areas.

2. Loss of tendons means that there is little prospect of restoring function, and immediate amputation will often be called for. Extensor tendons without much gap or fraying may be sutured, but if flexor tendons are divided, the chances of recovering any useful movement are often much reduced, especially in contused or lacerated wounds.

3. Disorganization of joints means that the affected finger will be stiff, and will prevent proper closure of the hand, and in addition the stiff finger will constantly be exposed to injury.

4. The ideal sites for section are disarticulation of the terminal phalanges, or amputation through the shaft of the metacarpal. Short stumps are of little value, especially in the case of the index and the little fingers. Stumps of the middle and ring finger may be useful if they are flexible and long enough to support the remaining fingers, and are not painful.

5. In the case of the thumb, length should be preserved as far as possible. Excision of joints is feasible in cases which require it, since a stiff thumb is certainly better than no thumb at all. If ankylosis or synostosis after portions of the bones have been removed is unavoidable, the aim should be to secure that position which will enable the thumb to be opposed to the fingers.

6. There need be no hesitation in removing the head and distal part of a metacarpal shaft. As emphasized by Bailey (1936), this procedure does not weaken the hand, and the cosmetic result is far superior.

7. Very severe injuries, with much loss of skin and division of the blood vessels and nerves, usually demand immediate amputation. Skin loss alone may be restored by grafting.

8. If infection is already present when the case is first seen, disarticulations are preferable to amputation through bone.

Anæsthesia in hand operations

Intravenous barbiturates or gas-oxygen are safe and give satisfactory results. Brachial plexus anæsthesia is time-consuming and somewhat uncertain in action. As it is apt to cause a considerable fall in blood pressure, it should be used with caution in shocked patients. Patients with hand injuries may have other injuries as well. Regional anæsthesia may be employed in certain cases by blocking the median and ulnar nerves in the vicinity of the elbow. Local infiltration is not recommended. It increases the risk of infection, and there is a slight but distinct risk of gangrene from persistent vasospasm, and therefore, if used at all, the mixture should contain no epinephrine. An Esmarch tourniquet may be used in 'cold' amputations, but in fresh or infected cases it is better avoided, the vessels being seized by hæmostats as encountered, and hæmorrhage may be diminished by temporary digital compression of the main vessels.

Amputation of whole finger

The incision used should be of the modified racquet type, and it should be eccentrically placed so that the handle of the racquet lies to one side of the metacarpal to be divided, so that the distal part of the scar is kept away from the web. This manœuvre vastly improves the cosmetic result. In fact, the casual observer often fails to notice that one finger is missing, after this is done. The head and at least one-third of the metacarpal shaft should be removed, but in the case of the index and little finger, the bone should be divided obliquely somewhat more proximally, so that no ugly projection remains evident (figure 1).

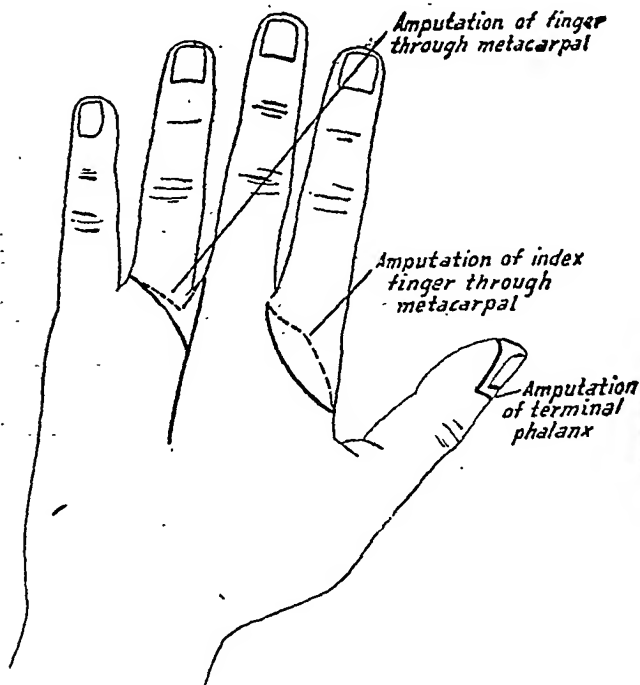
Buried sutures should be avoided as far as possible, and the skin should be united by very fine interrupted nylon sutures which should be removed early. Digital nerves should be sought and pulled down and divided squarely with a sharp scalpel. Firm bandaging, in allowing the tissues to fall together, helps to obliterate the space.

Fish-hook wounds

It is an unpleasant duty to advise patients to part with index fingers which had become painful and useless following infection originally caused by a fish-hook. The hooks used in

artificial flies are usually small and clean, and the hackles tend to prevent deep penetration. Larger hooks used for bait are especially dangerous, as they often have decaying organic matter adhering to them, particularly in the angle of the barb. The advice that the hook should be pushed through the finger till the point emerges from another place so that it can be

Fig. 1.
Incisions for finger amputations

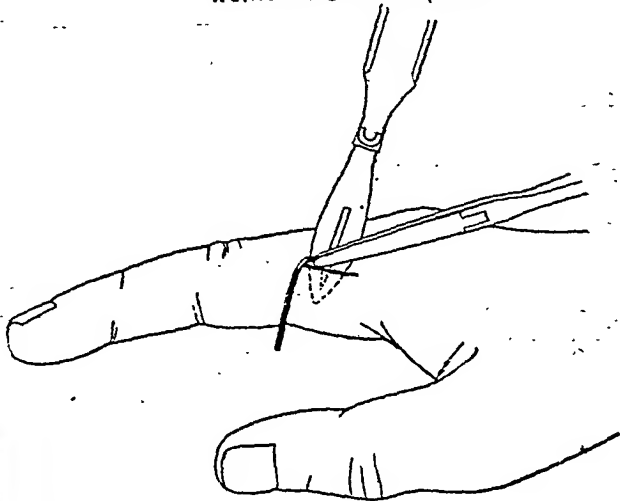


withdrawn point first is another instance of a claim which has been copied from textbook to textbook and from paper to paper. It is a very dangerous procedure. Not only is more infective matter likely to be carried in, besides the risk of leaving in what is caught under the barb, but unnecessary extra trauma is inflicted. Hooks vary in design especially with regard to the shape of the bend and the offsetting of the point, and it is not possible accurately to forecast where the point will emerge, or whether it will pierce a tendon sheath or not.

Surgeons unfamiliar with fish-hook design might be rewarded by studying a tackle manufacturer's catalogue. If the hook is already deeply driven in, it may be justifiable to push it out point first, but in the majority of cases the barb is caught just under the skin further progress having been arrested by the bend of the hook. It should be withdrawn the way it went in with a minimum of additional trauma. This can be done by slipping a small blade alongside the point of the hook with the edge facing the shank. The hook and blade are then seized in a hæmostat together, and the hook is rotated till the barb is felt to be in contact with the side of the blade and then both can be withdrawn

together (figure 2). The small incision may then be allowed to bleed for a while to carry out infective matter, and then treated with sulphanilamide or some other bacteriostatic agent, and dressed. Severe sepsis may follow fish-hook wounds, and it should carefully be watched for, and chemotherapy should be instituted in the hope of suppressing infection.

Fig. 2.
Removal of fish hook



Diphtheroid infections

In the earlier years of the war we encountered a number of patients suffering from wounds of the hand from which diphtheroid organisms were recovered. These wounds have no very characteristic appearance, but they are very chronic, and discharge pus in large amount. The pain is often very severe and not confined to the wound itself. Often there is a peculiar characteristic stinking odour not unlike that of gas gangrene, which together with the severe pain enabled us to recognize the condition clinically.

The pain is evidently due to an ascending neuritis, and in some cases persists after the wound has healed, or after amputation. In long-standing cases, severe and persistent pain in a functionless hand is apt to result in psychoneurotic symptoms. Two of our patients actually became insane.

True wound diphtheria has been encountered as well, especially in association with epidemics of faucial diphtheria, and some of the patients exhibited such sequelæ as myocarditis and motor paralyses.

Treatment should be prompt and effective. Neither sulphonamides nor antitoxin appear to have much effect on the local infection, but, in view of the danger of overlooking true wound diphtheria, antitoxin should certainly be given without delay and without further bacteriological report.

The most effective local treatment has been the application of 'Bipp' paste or the actual cautery. We have had no opportunity of treating any of these cases since penicillin has become available.

Burns

Dupuytren's classification of the degrees of burns dies hard. It is not only obsolete but entirely misleading, because it rather tends to suggest that the tissues are destroyed or damaged in orderly centripetal progression. This is certainly not the case. The hands are essentially small masses of tissues with a relatively large surface of skin. Unlike the trunk, heat may be applied on both sides, and readily penetrates.

It is therefore important to realize that, even with comparatively mild burns, considerable trauma may be offered to the deeper tissues sufficient to result in arthritis, osteitis with decalcification recognizable radiologically, peritendinitis and thrombosis of the veins. The possibility of such complications must be recognized, and one should not be in a hurry to blame the treatment used in the event of unfortunate results in which the damage has already been done by the burn itself. The writer has found the following classification of burns more useful in practice.

Class A.—Erythema. No treatment is necessary other than the application of emollients.

Class B.—Vesiculation. The prognosis is good and healing occurs in about twelve days with any treatment which is not actually harmful.

Class C.—Bullæ. Large blebs form, containing fluid with a high protein content. These blebs are the essential feature, but they readily burst leaving a moist red weeping surface. The epithelium is damaged to a critical degree.

Class D.—Any burn deeper than C. The epithelium is destroyed, and healing can only occur from the periphery.

For selected cases of hand burns, tanning is to be preferred, notwithstanding the fact that coagulation methods have recently waned considerably in popularity, and have even been forbidden in the army. *Where indicated and properly carried out*, the results of tanning have been so uniformly good that one becomes very loth to abandon a well-tried method until more definite therapeutic advances are made than the present 'new' methods which are actually the old methods reintroduced and combined with bacteriostatic agents. Tanning will give excellent results in B, and B and C burns of the hand and fingers, provided the cases can be kept under the close observation of a surgeon familiar with the method and its limitations. Its advantages outweigh the disadvantages. The coagulum should be obtained quickly, and should be thin and supple. This allows the fingers to be exercised from the start, a point of utmost importance, and when the coagulum separates off in about from ten to fifteen days, function is perfect, and there is no residual disability.

Rapid tanning is obtained by the use of dry powders. The use of solutions and the electric hair dryer nearly always causes contraction and ischæmia of the tanned area.

The burned area is cleaned with an antiseptic lotion, loose skin cut away or pushed aside and

the area very thoroughly dried by pressure with damp gauze or cotton. If the burn is very dirty or greasy, cleaning must be done under general anaesthesia, but otherwise morphine-hyoscine narcosis is sufficient. Oil and grease can be removed by cetavlon or pure dettol. The following powder is then very sparingly dusted on with a swab:—

	Per cent
Tannic acid	20
Talcum	20
Sulphanilamide	60

This produces an immediate coagulum which is very thin and supple, and since the total amount of powder which adheres even to an extensive burn is so small, the dangers of tannic acid or sulphanilamide absorption are negligible. This treatment has been tried in a number of cases of bilateral symmetrical burns of both hands and forearms. Whichever appeared to be the worse side of the two was tanned, and the contra-lateral arm used as a control and treated by some other method such as sulphanilamide cream. Greasy applications have serious drawbacks. Their bulk interferes with finger movement, the bacteriostatic effect of sulphanilamide is feeble and short-lived, and the skin becomes macerated. The infection rate is higher than with tanning. If sulphonamides are to be used at all, they should be given by mouth. With tanning it is advisable to administer sulphathiazole by mouth for four or five days as an additional safeguard, but we have had practically no trouble before we started using it. Neither have we a great deal of enthusiasm for 'triple dye' or other forms of chemotherapy. Those made up in a jelly base are particularly noxious. The coagulum is hard and the infection rate is high.

On the whole, far better and quicker results have been obtained by tanning. It is true that tanning has fallen largely into disfavour, but it is suggested that many of the unfortunate results which have received so much publicity have been due to errors of technique, and to neglected infection. In circumstances under which the patients cannot be closely watched and preferably by one surgeon, e.g. peak casualties during warfare, coagulation must be replaced by those methods which are capable of doing the least harm. The danger of tannic acid causing liver necrosis is a comparatively small one when limited areas are tanned, but it is one which must be recognized, and should be looked upon as an indication for caution rather than as an absolute contra-indication. Though the place of tanning in burn surgery has been attacked with some vigour, it has had a number of defenders, and as recently as 1944 Franklin in a carefully-balanced paper points out that tanning still has a considerable sphere of usefulness in certain cases and under certain circumstances, but emphasizes that no one

method of treatment is suitable for every burn under every set of conditions. He draws attention to the need for a better understanding of the principles of burn therapy as opposed to rigid adherence to one particular method.

Small areas of deep burning may be allowed to heal under a coagulum. Tanning is not suitable for extensive burning of class D, nor for circumferential burns, not because the coagulum constricts the blood supply but because circumferential burns of the fingers or hand are always class D on the dorsum where the skin is thin, and bone, tendon, and joint lie unprotected by adipose tissue. Grafting is imperative, and poor results will follow any other procedure. The hand must be prepared for grafting as early as possible by means of antiseptics, and perhaps the best means of achieving this is to use the Bunyan envelope and irrigation with hypochlorite solutions.

Split skin grafts are indicated in burns of moderate depth, or in deep burns of moderate extent. The grafts can be held in place by strapping on slabs of sterilized sponge rubber with elastoplast, and some movement is permitted which does not interfere with the 'taking' of the graft. Large burns exposing the tendons require whole skin plus some fat. This means a pedicled or tubed graft; or a band of skin can be lifted from the abdomen and the hand kept under it till it adheres, and the edges can be cut free and sutured to the edges of the defect. With this type of graft, the cosmetic results often fall short of ideal, but the functional results are superior to those obtained by the use of split skin grafts.

Deep burns of the dorsum of the hand, which have been allowed to heal by cicatrization, or over which too thin a graft has been applied, often show a less acceptable result when examined a few months after the patient has been discharged, increased stiffness, contracture, and blisters being not very uncommon sequelæ. Whatever method is used, surgical treatment should cease only when full, or at least the best possible, function has been restored permanently. This period does not necessarily coincide with the period of wound healing.

Summary

1. The treatment of septic infections of the fingers has been discussed.
2. The indications for conservative and radical surgery of hand wounds with special reference to war wounds have been discussed.
3. The technique of finger amputations has been described.
4. A simple method of extracting fish-hooks has been given.
5. Diphtheroid infections have been described with reference to management.
6. The pathology and treatment of burns of the hand and fingers have been discussed.

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SOME EXPERIENCES WITH PENICILLIN

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1. Bacteriological (Dr. J. T. Cornelius)

IN December 1944, penicillin was made available to the hospital by the surgeon-general with the Government of Madras for clinical trial, and since March 1945, it has been purchased in the open market.

The following report relates to the results and experience gained in the use of penicillin in the treatment of selected cases of infection which were sulphonamide-resistant, and caused by organisms that were penicillin-sensitive on bacteriological tests.

In the bacteriology laboratory, Fleming's agar-cup method was adopted for determining the penicillin sensitivity of the organism. The method consists in puncturing one or two circular holes in a blood-agar plate with a sterile cork borer, and after inoculation and spreading, a drop of weak penicillin (10 μ and 1 μ per c.c.) is pipetted into each hole. The inoculated plates are incubated. Penicillin diffuses through the media and produces zones of inhibition from the centre of the hole. The distance of the inhibition zone from the centre is taken as a measure of the sensitivity of the organism.

In a few cases, the penicillin content of exudates was also estimated by placing it in a cup in an agar plate which was heavily inoculated with *Staphylococcus aureus* and noting the distance of the zone of inhibition from the centre. This gave a measure of the concentration of penicillin in the exudate. By this method, the effect of penicillin was found to persist even after 48 hours of treatment.

Penicillin sensitivity tests were carried out on micro-organisms isolated from blood cultures or cultures from infected areas when they are considered to belong to the group of penicillin-sensitive organisms. Suitable cases were thus selected for penicillin treatment.

Penicillin was obtained as the sodium salt. It is a brown yellow powder put up in vacuum vials of one hundred thousand units. It is extremely soluble in water and saline. The sealed vials containing the dry powder are stored in the refrigerator until they are used, as the potency of penicillin is affected by high temperatures. The potency is measured by the amount of penicillin which completely inhibits the growth of a test strain of *Staphylococcus aureus* which is termed the Oxford unit.

Twenty c.c. of sterile saline is introduced with a sterile syringe through the rubber cap of the vial with aseptic precautions. This gives a solution of 20 c.c. containing 5,000 units per c.c. These vials containing the solution are also placed in the refrigerator during use, and they were used up within 24 to 48 hours of preparation. Three to five c.c. of this solution were injected intramuscularly at 3-hour intervals into the patients under penicillin treatment.

Penicillin cream was made with solutions containing 500 to 1,000 units per c.c. for local use.

II. Clinical (Dr. Carol E. Jameson)

In the Medical College Hospital at Vellore, we have had the head of the bacteriology department and one of the clinicians in charge of all our penicillin treatments, in collaboration with the doctors in the various departments. Forms are furnished by the surgeon-general's office requiring data regarding bacteriological findings and accurate information on time and manner of dosage of penicillin, with clinical results in relation to this. At first, penicillin sensitivity tests were required in all cases. Later, since it has been recognized that staphylococcus is almost universally responsive to penicillin, we have sometimes used it in these cases without waiting for sensitivity tests. Since the ban has been off in venereal cases, we have had a few gratifying results with gonococcus infections. When cases slip back, or fail to continue their initial good response, a second bacteriological examination usually shows a secondary invader or a loss of sensitivity of the original organism, usually the former. A few of our cases have been treated on the basis of sputum cultures or cultures taken from the cervix uteri, in which we have not been absolutely certain that the cause of the patient's prostration was due to this source. Usually the results have justified its use, although lack of sufficient penicillin in some cases accounts for failure to sustain initial improvement.

I shall try to analyse our cases briefly, giving our most definite and unquestionable results first. In some cases, when we felt we were about to lose the patient, we took the culture and began treatment after smears, pending a blood or other culture.

I. A baby, aged 4 days. Admission 5-4-45.
Diagnosis: Ophthalmia neonatorum.

Bacteriology: 9-4-45. Eye smear—gonococcus.
15-4-45. Eye smear—negative.

Treatment: 9-4-45 to 14-4-45. Saline irrigations, 2 per cent silver nitrate, M&B 693 ointment, M&B 693 by mouth. 14-4-45, 11 a.m. Penicillin 500 units per c.c., 2 drops 2-hourly and vaseline to lids. 15-4-45. Penicillin 3-hourly.

Clinical course: Before penicillin treatment, the eyes were getting progressively worse, lids and surrounding tissues so swollen it was impossible to see the cornea without retractors.

Result: After penicillin, within 24 hours the eyes looked normal.

II. A woman, aged 22. Admission 14-4-45.
Diagnosis: Puerperal sepsis and severe anaemia, nephritis.

Bacteriology: 23-4-45. Uterine culture—staphylococcus. Blood culture—negative.

Treatment: Sulphanilamide 6 tablets. Sulphaguanidine 34 tablets. Liver extract 6 injections, blood transfusion, and intravenous glucose and diuretics. 23-4-45. Penicillin 100,000 units in six 3-hourly doses for 24 hours only.

Clinical course: The patient was getting progressively worse; haemoglobin 17 per cent; temperature 102.4°F.; suppression of urine; eyes swollen and shut. A severe diarrhoea had been controlled by sulphaguanidine.

Result: Immediate improvement within 24 hours followed 100,000 units of penicillin after which it was stopped, and improvement continued.

III. A woman, aged 20. Admission 21-2-45.

Diagnosis: Puerperal sepsis—breast abscess.
Bacteriology: Blood cultures aerobic and anaerobic—negative. Cervical smear—streptococcus. Breast abscess culture—*Staphylococcus aureus*. Urine culture—*B. coli* and *enterococcus*.

Treatment: Sulphanilamide tablets 12, M&B 693, 9, sulphaguanidine 18, blood transfusion 200 c.c. 28-3-45. Penicillin 3-hourly, 15,000 units for 3 days—total 350,000 units. After a 4-day interval 650,000 more units, 15,000 every 3 hours over a period of 6 days. Total 1,000,000 units.

Clinical course: After a normal delivery temperature 100°F. Haemoglobin 20 per cent, red cell count 728,000, normoblasts present. Haemoglobin continued to drop after delivery. A blood transfusion of 200 c.c. followed by a severe reaction with fever to 104°F. Six days later, haemoglobin 13 per cent with fever, diarrhoea and vomiting. Sulphaguanidine used, but stopped because of vomiting. Oedema of face increased. Penicillin started.

Result: Rapid improvement with loss of toxic symptoms and reduction of oedema about the eyes. After 3 days of penicillin (i.e. 350,000 units), stopped. After 4 days, it was evident that she was slipping back, and 650,000 more units were given. This time, the improvement was permanent. The baby is flourishing.

Discussion: The appearance of the breast abscess was that of a metastatic abscess. The breasts were empty, absolutely flat, and there was no generalized or localized mastitis. I believe the cervical smear and urine cultures can be disregarded. *Staphylococcus aureus* was probably the causative organism and the breast abscess was not the source of the toxæmia but only a local fixation abscess indicating the real nature of the infection.

IV. A patient, aged 35.

Diagnosis: Cellulitis of face. Septicæmia. Diabetes.

Bacteriology: 20-2-45. Smear from lip pustule—*Staphylococcus aureus*. 21-2-45. Blood culture—*Staphylococcus aureus*. 27-2-45. Blood culture—negative. Pus from pustule on lip; streptococci in short chains.

Treatment: Full doses of 'Cibazol' and 'solu-septasine' were given for 48 hours, also insulin to control the diabetes. The patient became progressively worse. It was almost impossible to see the cornea by separating the eyelids, because of oedema, which extended over the top of the scalp. The temperature ranged between 102°F. and 103°F. Penicillin was started when the patient was becoming progressively worse. A total of 1,100,000 units was given in doses of 15,000 every 3 hours.

Clinical course: The temperature dropped to 99.6°F. within 3 days and the swelling gradually subsided, leaving a dozen localizing pustules over lips, cheeks, and scalp. These subsided without surgical interference and the temperature was normal in 2 weeks.

Result: Complete cure.

V. A patient, aged 58.

Diagnosis: Diabetic carbuncle.

Bacteriology: 15-3-45. Culture from pus—penicillin-sensitive *Streptococcus* and *Staphylococcus aureus*. Blood culture—negative.

Treatment: Sulphathiazole and insulin. Penicillin 15,000 units every 3 hours—200,000 units.

Clinical course: Marked improvement after penicillin.

Result: Immediate improvement. 28-4-45. A huge scar had almost closed completely.

VI. A patient, aged 55.

Diagnosis: Cellulitis of face from abscess at inner canthus left eye.

Bacteriology: Culture from abscess—*Streptococcus hæmolyticus* and *Staphylococcus aureus*. Blood culture—sterile.

Treatment: One hundred and twenty-two sulphathiazole tablets were given—2 tablets at 4-hour intervals.

Temperature was still 103.8°F. with daily chills. Penicillin 300,000 units given.

Clinical course: A generalized eruption resulted from sulphathiazole sensitivity, and both ears were involved in a swelling which looked like erysipelas. Temperature 103°F., and delirium continued. Urine showed sugar. After 300,000 units of penicillin given, 15,000 units every 3 hours for 3 days, his temperature was normal and toxæmia gone.

Result: Rapid recovery.

VII. A woman, aged 34.

Diagnosis: Ruptured ectopic gestation—toxæmia—pneumonia.

Bacteriology: Sputum culture—penicillin-sensitive streptococci.

Treatment: Laparotomy with the removal of ruptured tube, and autogenous transfusion. Sulphathiazole 2 tablets every 4 hours for 3 days. M&B 693 every 4 hours for 3 days. Oxygen inhalations. Penicillin 60,000 units at 10,000 units every 3 hours for 6 doses.

Clinical course: The patient was admitted with bowels acutely distended with gas, and the abdomen full of blood, with an influenza-like cold and cough with temperature of 100°F. Emergency ectopic operation was done and auto-transfusion. Distension made it difficult to return the bowels to the abdomen. Cough grew worse after operation with severe dyspnoea and thick yellow sputum. The abdominal distension had subsided, so the dyspnoea was not due to that, but it increased throughout the first week post-operative, with signs of pneumonia in the left lung. She was too ill to be taken to the x-ray room until later when the film showed a resolving pneumonia. Oxygen was given intermittently, 29-12-44. The dyspnoea was severe enough to suggest a pulmonary embolism.

After 60,000 units of penicillin, 10,000 units every 3 hours for 6 doses, the condition improved rapidly. Temperature was normal in 4 days, and she was discharged within 9 days.

It is of interest to note that this was the eighteenth pregnancy. All the previous ones ended in toxæmia and miscarriage. The one preceding this was particularly severe, with a blood pressure of 220/140.

Result: The patient was discharged on the 21st day in good condition. The dose of penicillin was unbelievably small, but I believe tipped the balance between life and death. Similar reports have appeared elsewhere.

VIII. A medical man.

Diagnosis: Abscess of finger.

Bacteriology: 16-3-45. Smear—*Staphylococcus aureus* and streptococci, culture from pus, *Staphylococcus aureus*.

Treatment: Sulphathiazole by mouth. Incision and drainage, but it did not drain freely. Penicillin 255,000 units, 15,000 every 3 hours, and 15,000 applied locally at intervals in a cream. Total 270,000 units.

Clinical course: Toxæmia continued in spite of sulphathiazole by mouth and incision. The whole finger remained swollen and there was no tendency to localize after penicillin treatment for 3 days, the finger looked much better and the toxæmia subsided.

Result: Good. The abscess was covered with a delicate scar 15 days after treatment.

IX. A patient, aged 25.

Diagnosis: Cellulitis of arm.

Bacteriology: 15-3-45. Smear from pus—*Staphylococcus aureus*; blood culture—negative.

Treatment: Sulphathiazole by mouth. Incisions. Penicillin 15,000 units every 3 hours. Total 500,000 units.

Clinical course: Marked toxæmia and high temperature until 3 days after penicillin. X-ray of the right humerus showed only thickening of the periosteum.

Result: Cure. 30-4-45. No pus, but skin not yet closed over granulation tissue.

X. A woman, aged 21.

Diagnosis: Chronic gonorrhœal cervicitis and salpingitis.

Bacteriology: Cervical smears and cultures showed gonococci.

Treatment: 4 T.A.B. vaccine intravenously starting with 1 c.c. and increasing to 4 c.c. with febrile reactions to 103. Sulphathiazole 66 tablets. Gonococcus vaccine 20 millions, 40 millions and 50 millions. No improvement.

Clinical course: The profuse irritating yellow discharge continued. No trichomonas was found. Penicillin 200,000 units given at 15,000 every 3 hours and 1 c.c. locally into the cervix with the patient in the Trendelenburg position, followed by a vaseline tampon in the vagina given twice. A laminaria tent was also put into the cervix to help drainage. Medical diathermy was given—120°F. for 10 minutes, to cervix. This increased the profuse watery discharge temporarily.

Result: Marked improvement.

XI. A patient, aged 22.

Diagnosis: Crushed of the leg below the knees.

Bacteriology: No culture before operation. Culture from wound after operation—*B. pyocyaneus* and *B. coli*. No gram-positive organisms after treatment.

Treatment: Removal of leg by severing tissue (patient was in shock). Amputation of ragged ends 2 days later. 78 tablets of sulphathiazole and 2 transfusions 200 c.c. and 150 c.c. given; 312,000 units of penicillin given prophylactically, 34,000 locally to the wound and 278,000 parenterally.

Clinical course: This is the only patient treated prophylactically with penicillin. After the last injection, the penicillin content of blood was tested and showed about 2 units per c.c. This is the only case in which we tested the penicillin content of blood.

Result: Good. The surgeon believed that the case would have been very much prolonged had the penicillin not been used. The temperature came to normal within 2 weeks.

XII. A child, aged 1½ years.

Diagnosis: Unresolved pneumonia.

Bacteriology: Sputum culture. Penicillin-sensitive pneumococci.

Treatment: M&B 693 by mouth, ½ tablet doses. A greater amount was given than for the average case of pneumonia. X-ray still showed a large shadow at the left base. Penicillin 100,000 units, 5,000 units every 3 hours for 20 doses.

Clinical course: Toxæmia and fever continued in spite of treatment until penicillin was given. The temperature dropped to 99°F., but recovery was delayed by dysentery. X-ray treatment to the chest was also given for the unresolved pneumonia.

Result: The child was taken home against advice, very much improved. We believe this case showed a definite response to penicillin, but it was not so clear-cut as some of the others.

The three following cases showed a definite response to penicillin treatment, but we believe that in all three further surgery is indicated to remove the focus.

XIII. A patient, aged 17.

Diagnosis: Multiple osteomyelitis.

Bacteriology: Blood culture—negative. Smear from sinus, *Staphylococcus aureus*.

Treatment: Penicillin 15,000 units every 3 hours for 14 doses. 12,500 units every 3 hours, 3rd and 4th days, and 10,000 units every 3 hours, the 5th day to a total of 500,000 units, following repeated surgical procedures and sulpha drugs by mouth.

Clinical course: Toxæmia improved at once after penicillin; temperature dropped from 103°F. to 99°F. It rose again after an interval of a few days.

XIV. A woman, aged 25.

Diagnosis: Cystitis—pneumonia, thrombophlebitis.

Bacteriology: Urine—gram-negative rods. 11-4-45. Sputum—pneumococcus and *Micrococcus catarrhalis*. Urine culture—streptococci and *Micrococcus tetragenus*. Urine culture—sterile. 17-4-45.

Treatment: Bladder irrigations with 1/4,000 acriflavine 5 days and sulpha drugs. Penicillin 900,000 units at 15,000 units every 3 hours intramuscularly.

[Dec., 1945]

Clinical course : Copious sputum throughout. X-ray showed probable bronchiectasis of both bases. After penicillin the thrombophlebitis improved at once. The pain and swelling in the left thigh was reduced and the toxæmia improved. The sputum continued and the temperature remained low.

Result : Indeterminate. I believe this should be definitely a case for lobectomy, if one sided. After lipiodol studies this might be done now on the worst side.

XV. A woman, aged 48.
Diagnosis : Hydro-ureter, ulceration of the bladder.
Bacteriology : Urine culture—*Streptococcus hæmolyticus*. Urine smears—no acid-fast bacilli.
Treatment : Penicillin previously given elsewhere parenterally 1,000,000 units. 5,000 units given into the bladder here with temporary improvement on two occasions.

Clinical course : Very painful attacks right loin and iliac region coming in spasms about every 2 days and requiring morphine for the past 1½ years following a right nephrectomy for septic kidney. She was told that there was no extensive lesion in this kidney. Cystoscopic examination now shows ulceration above the right ureteral opening. She localizes her pain here. There is a low-grade cystitis throughout the bladder, and both ureteral openings gape slightly.

The four following cases ended in death, although three of the four showed initial improvement and might well have recovered with massive doses. Three showed septicæmia and one a generalized peritonitis.

XVI. A woman, aged 32.
Diagnosis : Peritonitis following criminal abortion.
Bacteriology : Culture of pus from abdominal cavity. *Staphylococcus aureus* and *pyocyaneus*, 21-4-45.
Culture from cervix—gram-negative bacilli, 26-4-45.

Treatment : 21-4-45. Drainage through laparotomy wound, of a profuse generalized cloudy watery exudate with thick pus (foul smelling) welling up from the pelvis, after breaking light adhesions. Suction was applied and about two quarts obtained. In spite of the probable presence of *B. coli*, 1 c.c. of penicillin of 5,000 units was put into the peritoneal cavity. Soluble sulphanilamide 1 ampoule 5 grammes given intravenously with saline and glucose during the operation. Wangenstein suction and intravenous glucose and saline given intermittently after the operation. 500 units was put into the drainage tube and the drainage tube clamped for 4 hours, in order to retain it in the peritoneal cavity. Sulphathiazole 1 g. was given every 4 hours by mouth. 25-4-45. 500 units were put into the peritoneal cavity through the drainage tube, 3 doses only, 15,000 units intramuscularly.

Clinical course : The patient had a history of 5 days' lower abdominal pain. The day following admission the patient got rapidly worse, was cold, clammy, and pulseless with a white blood cell count of 9,000 and temperature of 99°F. The abdomen was tender and by vaginal examination the posterior cul de sac was full and tender but no mass felt. The systolic blood pressure was 70. The patient was bleeding slightly from the vagina, was thirsty and restless, and the pulse almost imperceptible. The history of amenorrhœa followed by an attempted abortion suggested to be by medical means, the month previous, suggested criminal abortion. The history of a fair amount of bleeding at home was against the diagnosis of ectopic gestation, but the clinical signs were very suggestive, so we explored under local anæsthesia with a possible diagnosis of ectopic pregnancy. The odour of the pus obtained on opening the abdomen made us feel the penicillin was probably useless, but we used 1½ c.c. here (7,500 units) locally, although we felt that *B. coli* and *pyocyaneus* probably contradicted it.

The patient went off the table warm and with a very much improved pulse. The temperature rose to 103°F., the patient was hungry, bowels moved, and

improvement seemed marked. The following days there was almost no discharge from the wound. Suddenly on the evening of 26-4-45 her pulse became very poor again, she became cold and clammy, developed internal strabismus and dyspnoea. The three doses of penicillin by injection were given only after she became moribund.

Post mortem : Showed the abdomen almost free of pus with no localized reservoir and the bowel surface more normal than at operation. The peritonitis appeared to originate in a broad ligament abscess now empty of pus. The uterus contained products of conception of about two months' duration. Examination of the head was not permitted.

Comment : We believed the patient was recovering without penicillin when she became suddenly worse and died.

XVII. A woman, aged 22.
Diagnosis : Puerperal septicæmia. Pneumonia, meningitis.

Bacteriology : Blood culture—*Streptococcus*, 22-2-45. Sputum culture—*Streptococcus*. Spinal fluid culture—*Streptococcus*. All were penicillin-sensitive.
Treatment : Sulphanilamide; then sulphydrydine; then sulphathiazole; then penicillin. Blood transfusion 300 c.c. Penicillin 12,500 units every 3 hours for 30 doses after an interval of 3 days, 15,000 units every 3 hours for 14 doses. Total—540,000, intrathecal 10,000 units.

Clinical course : In spite of extensive sulpha drug therapy, the patient became semi-comatose and developed a positive Kernig's sign. The meningeal symptoms improved within 24 hours after parenteral injections of penicillin, even before the single intrathecal dose. The general condition improved markedly until we stopped, after 340,000 units. She then became worse and did not improve after her second dose of 210,000 units. She became extremely anæmic and dyspnoic. Her lung condition remained the same and pulmonary oedema developed shortly before her death with some cardiac dilatation. There was no return of the meningeal symptoms.

Result : Death.

Comment : Insufficient dosage of penicillin and lack of more blood transfusions were probably responsible.

XVIII. A man, aged 26.
Diagnosis : Staphylococcal septicæmia with peritonitis.

Bacteriology : 1-2-45. Blood culture—*Staphylococcus aureus*. 19-3-45. Blood culture—*Staphylococcus aureus*. 19-3-45. Pus culture—*Staphylococcus aureus*, *hemolyticus*, *pyocyaneus*, and *B. coli*.

Treatment : Sulphathiazole was given for 24 hours with no result. Then penicillin 15,000 units every 3 hours for 22 doses, a total of 330,000 units.
Clinical course : On admission he was delirious with a temperature of 103°F., vomiting, and restless with distended abdomen. He became conscious and less toxic immediately after penicillin treatment. A large incision permitted a drainage of a large quantity of pus from the left loin and thigh. Pus continued to pour out, a faecal fistula developed, abscesses developed elsewhere. The pus was foul smelling. 19-3-45. Six weeks later, patient was obviously going down hill. Penicillin was given again intravenously and intramuscularly in 20,000 unit doses for 24 hours with no result.

Result : Death. I believe an insufficient dosage in the beginning was responsible for his death.

XIX. A woman, aged 35.
Diagnosis : A huge lung abscess.
Bacteriology : Culture from sputum—*Staphylococcus aureus* and *hemolytic streptococci*; penicillin-sensitive.
Treatment : Parenteral 5,000 units per dose for 4 doses and 10,000 units per dose for 6 doses. Total—80,000 units.

Clinical course : Fever and toxæmia were marked; sputum profuse and foul smelling. After 36 hours' treatment there were no signs of improvement. The patient became extremely dyspnoic and cyanotic and died almost at once.

Result: Death. After death, a sterile syringe drew out from the lung pus with penicillin-sensitive staphylococci. The symptoms suggest a rupture of the pulmonary abscess into the pleural cavity. Post mortem refused.

XX. A woman, aged 55.

Diagnosis: Diabetes and post-operative sinus.

Bacteriology: *Staphylococcus* and *pyocyaneus* in culture from sinus.

Treatment: After a month of treatment with various antiseptics and curetting of the wound, it finally closed after injections into the sinus of washings from an empty penicillin bottle!

Clinical course: The sinus in the abdominal wound followed the removal of a large extensively adherent multiple endometrial cyst together with a hysterectomy. The tumour had to be dissected, from the bowels on all sides. The sinus followed a wound infection. As the patient was very fat, this was quite deep.

Result: Healing. Our results bear out the well-known fact that penicillin is very potent in cases with sensitive organisms and adequate drainage.

No toxic effects or reactions such as thrombosis of veins, fever and local irritations were observed. Very few injections were given intravenously. There seem to have been no injuries to kidneys, liver, bone-marrow or nervous system. We used it intraspinally in meningitis cases on two occasions with also generalized blood infections. No cutaneous rashes occurred. Penicillin was used successfully in infections due to *Staphylococcus aureus*, streptococcus, pneumococcus, gonococcus and anaerobic streptococcus. Cases came from both the medical, surgical and obstetrics sections, and to them our thanks are due.

A CASE OF PERI-DUODENITIS WITH DUODENAL STENOSIS AND TRACTION DIVERTICULA

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SPAGNOLIO FRANCESCO, M.D. (Milan)

AFTER the exhaustive papers on the subject by Kellog (1933), and Kraas and Beck (1934), and several reports of cases by various authors following the work of Case, it would appear useless to report any further cases. The present one is reported only in view of its very peculiar features and pathogenesis.

History.—In 1936 the patient, a male, aged 56, suffered from a cold tuberculous abscess starting from the 8th dorsal vertebra. He was then put in plaster for 2 months and in an orthopaedic corset for another 4 months. In May 1943, a caseous abscess was opened in the right paravertebral region at the level of the first lumbar vertebra, and the patient was immobilized again for 4 months. From September 1943 to October 1944 the patient complained of intermittent stabbing pains in the epigastrium, occasionally diffusing to the back, without any relation to meals, especially occurring during the night for a period of 1 to 2 hours and accompanied by nausea and occasional bilious vomiting. Vomiting did not relieve the symptoms. During the last 2 months of 1944, the patient's symptoms increased in frequency and severity; during the first months of 1945, his troubles became continuous.

The pains were then cramp-like, starting in the right hypochondrium and extending to the back, occasionally to the right shoulder and to the lower part of the lumbar spine, and were present most of the day and night. The patient used to refuse any solid food and seek relief in frequent lavages of the stomach and injections of morphia, by which pain was only temporarily suppressed, while it was only relieved by atropine. Habitual constipation, loss of strength and weight (30 lb.). The genupectoral position and Haye's devices did not relieve the pain. Later his vomiting became almost continuous, and the vomit was always tinged with bile. The patient was then sent for surgical treatment to a surgeon, whose report is unfortunately not available. The patient never showed any temperature.

Examination.—Very poor general condition. Offensive breathing, tongue coated. Skin and conjunctivæ pale. Deformed scar in the right paravertebral region between the 12th dorsal vertebra and 3rd lumbar vertebra.

Respiratory system: few rhonchi scattered all over the lungs.

Circulatory system: heart area within normal limits. Second aortic sound accentuated. Blood pressure 120/80.

Abdomen: right hypochondrium and lower part of the epigastrium slightly tender at pressure.

Examination of the nervous system: negative. Spine: the spinous processes are tender on pressure in the lower dorsal region, which is rigid.

Examination of the gastric function shows extremely variable content of the fasting stomach (from 1-2 cm. to 1-2 pints of fluid). Mucus, starch, bile ordinarily present, blood absent. Lactic acid is not present. Vomiting contains rarely blood and frequently undigested food. The acidity curve is of high, continuous type (maximum 110 free HCl, 130 total acidity in 2 hours fractional extraction); the examination of the deposit shows only sarcinae and few red blood cells.

Blood urea: mg. 34 per 100 cm. of plasma (? chloropenic). Blood sugar: mg. 100 per 100 cm. of plasma.

Examination of stools, blood, urine, etc., revealed nothing of importance.

An x-ray of the spine showed evidence of an old caries of the 8th dorsal vertebra upper aspect, and of marked irregularity of the lower edge of the 1st lumbar vertebra. There were definite osteoarthritic changes in the lower dorsal and lumbar regions of the spine. A radiological study of the gastro-intestinal tract after a barium meal showed a hypertonic stomach of normal outline, size and shape, with marked mucosal pattern. There was some gastric residue in the 4th control, but no evidence of stenosis of the antero-pyloric area. Duodenal cap directed backwards. Diverticular pouches were visualized in the part of the duodenum, near the concave border, tender on pressure. The duodenal loop, at the level of its second flexure, was enlarged and tender, and showed deep mucosal pattern and peristaltic waves. Stasis had been detected in the diverticular pockets and in the enlarged loop. Radiological conclusions: moderate pylorospasm, diverticulosis with peridiverticulitis of the second portion of the duodenum, and stenosis probably secondary to adhesive peritonitis.

The mild pylorospasm is amenable to atropine, morphia and an oral dose of 20 mg. of benzedrine.

As it is easy to exclude a reflex pylorospasm from lesions of the appendix, gall-bladder or kidneys, the continuity of the symptoms, the attacks of bilious vomiting, the absence of relation between pains and meals, the presence of bile in the fasting gastric juice well fit in with the picture of a chronic duodenal obstruction (Kraas and Beck, 1934).

It would take too long to exclude here all the congenital and acquired lesions of the head of

the pancreas and duodenum (intrinsic and extrinsic) capable of causing a duodenal obstruction. Two points are worth stressing in view of the increasing number of cases of duodenal obstruction of this type lately reported: (1) The absence of giardia intestinalis in the stools, as giardiasis may be a cause of duodenal obstruction through a chronic hypertrophic duodenitis (Kirklin, 1933). (2) The symptoms are not relieved with the Haye's devices or by the patient taking up a genupectoral position, as they are relieved in duodenal obstruction caused by compression of stretched arterial vessels (Wilkie, 1921). As diverticula are present, it would also be justified to think that they may be responsible for duodenal obstruction. In a typical case reported by Kellog (1933), a distended diverticulum was responsible for a duodenal ileus of chronic type with biliary obstruction.

Described more frequently by radiologists than diagnosed by clinicians, duodenal diverticula have lately received considerable attention. Walton (1930) has classified as follows the clinical pictures of diverticulosis of the duodenum: (a) silence of symptoms; (b) dyspepsia (flatulence, feeling of distension, nausea); (c) symptoms of peptic ulcer; (d) symptoms of chronic pancreatitis; (e) symptoms of mild, intermittent duodenal obstruction (jaundice, biliary colic). In our case, the continuity of the symptoms and especially the radiological picture come to our help in excluding the possibility that all the symptoms of chronic duodenal obstruction were due to traction diverticula of the concave, outer border.

It appears that, in our case, duodenal obstruction and diverticula (most probably present) are both the result of adhesive peritonitis. A cold abscess of the 8th dorsal vertebra, descending along the retroperitoneal tissue, must have involved the peritoneal layer, causing a diffused process of peri-duodenitis, especially of the 2nd and 3rd portion, with secondary retraction. The mechanism of formation of the obstruction appears clear.

The formation of the diverticula, primarily due to traction, must have been favoured by a mechanism of pulsion for the obstacle present at a lower level of the duodenum.

In this way we can explain the peculiar features of the case, which are:—

1. The occurrence of acquired secondary true diverticula from traction in the second portion of the duodenum.
2. Their unusual position near the concave border of the duodenal loop.
3. The slow, and for a long time silent, development of a chronic, progressive duodenal obstruction.

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SOME POINTS IN SURGERY OF THE THYROID GLAND

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ABOUT nine-tenths of simple goitres are adenomatous (Wheeler). How truly does this apply to the hill tribes who live in the ranges of the Karakorams to the north of Kashmir, where goitre is more or less endemic. In certain districts practically 90 per cent of the inhabitants are afflicted with the disease, yet continue with their daily work in their fields, toiling just as if these swellings around their necks were physiological rather than pathological. In most cases the goitres are adenomatous, though occasionally one comes across a purely cystic colloid tumour, or even more rarely one purely parenchymatous in nature. Those of the purely parenchymatous type respond to iodine therapy if treated sufficiently early, but the colloid cystic and adenomatous or nodular varieties require surgical intervention.

It is not my intention to discuss the etiology of the disease (which is still disputed) but to describe the surgical procedure adopted here in partial thyroidectomies or sometimes hemithyroidectomies necessary for most of the cases which come up for operation.

It is seldom that one meets with an early case of a small nodular growth. Those who do decide to have their goitres removed do so

either because their tumours have become too unsightly, or because, after many years, they are only just beginning to feel the effects of pressure on the trachea, or because they have been requested to do so by their wives. In any case, the tumour is nearly always large, and its removal is not always easy. The toxic nodular goitre is rare here, and our surgical experience is confined to the non-toxic variety.

The pre-operative treatment consists of 10 minims of Lugol's iodine a day for 3 days, with a careful watch for nervous or cardiovascular disorders. Forty-five minutes before the operation, morphia 1/6 grain and hyoscine 1/150 grain are given hypodermically. In two early cases local anaesthesia was used, but as the tumours were large and a considerable time was spent in the operation, the patients grew tired, and the anaesthesia began to wear off before the end of the operation. Since then I have always preferred a general anaesthetic. Unfortunately, there are no means for intratracheal gas and oxygen and ether here, and the open general method has been compulsory. The anaesthetist should, if possible, be shielded from the surgeon by means of a Wheeler's face screen.

The incision is made as low as possible in the neck (preferably in a crease of the skin) either on the side of the tumour or over both sides according to whether the tumour is unilateral or bilateral. For those arising from the isthmus of the gland (and these, in my opinion, are the most difficult) the incision is usually shorter and almost midway between the sternocleidomastoid muscles. The skin incision being completed, the platysma comes into view, and the surgeon must decide whether the goitre can be tackled through a vertical or a transverse incision in the fibres of the platysma. If the tumour is fairly large I personally go through the platysma transversely. To dissect up the skin and then to incise the platysma vertically requires more time. The vessels are then tied with fine catgut and skin-towels applied. The next layer is the deep cervical fascia covering the pretracheal muscles. Underneath the fascia, and lying on the muscles, may be seen the right and left anterior jugular veins. The fascia is incised and the veins divided between clamps and ligatured. As in the case of the platysma, the pretracheal muscles will have to be divided either vertically or transversely. Often, in large goitres, the muscles may be so stretched as to appear membranous. They may be divided transversely without danger of much retraction or haemorrhage. In very large goitres I have found it necessary to divide a part of the sternocleidomastoid muscle to give more room for dissection and ligature of the lateral thyroid veins. Underneath the pretracheal muscles the capsule of the gland (a thin layer of fascia covering the gland) comes into view. It can easily be picked up and divided and then pushed over

the substance of the thyroid with gauze. Care should be taken not to injure any veins running over the surface of the gland, beneath the fascia. Rupture of any such vessel causes troublesome haemorrhage and a waste of valuable time.

The superior thyroid leash of blood vessels is next sought for. It will be found lying over the medial aspect of the upper pole of the gland. It is wise to dissect the leash up as far as possible towards its origin from the external carotid, so as to avoid missing a branch which may possibly occur higher up. Personally, I use a Watson-Cheyne's dissector for this purpose. Having decided on the point of ligature, a thyroid dissector with an eye is passed under the leash and a ligature is drawn under and divided (figure 2, plate XXVI). The ligature is tied above and below, and the leash of vessels is severed by cutting down on to the dissector passed under the vessels. A double ligature above is a wise precaution. Now the superior pole of the gland will be found more or less free and can be dislocated. The fingers are passed over the lateral margin of the gland and the mass is gently lifted towards the middle line, when the lateral thyroid veins will become visible. Sometimes these veins are extremely large and engorged, and rupture of one may be a source of considerable anxiety to the surgeon. Each vein should be carefully isolated and ligatured. The common carotid artery will then be seen and felt pulsating in the depths of the wound.

The gland is again gently moved over towards the middle line, and the inferior thyroid artery and veins are sought for. The artery will usually be found under the inferior pole, entering the gland substance or running over its surface after passing beneath the common carotid artery. These inferior thyroid vessels are ligatured and divided as in the case of the superior thyroid vessels, and one may encounter more difficulty in doing so, especially in large goitres. This done, it will now be possible to lift the whole gland out of the wound and turn it over upon the isthmus. In cases for partial thyroidectomy I then place a ring of artery forceps on the capsule just below the line where the section is planned. Two or three are placed on the vessels running across the isthmus from the opposite side. The gland is then cut across above the forceps in a wedge-shaped manner, large bleeders being picked up with forceps during the section. If both the superior and inferior thyroid arteries have been ligatured properly, there is seldom much bleeding. Some surgeons prefer to cut vertically through the middle of the isthmus down as far as the trachea. If the isthmus is enlarged I do not practise this method, as it often causes rather troublesome haemorrhage from the trachea and tissues beneath. To avoid injuring the recurrent laryngeal nerve, it is wise not to

lift the gland out of the wound too much towards the mid-line, as the nerve may be dragged with it and injured during section of the gland.

The cut edges of the remaining gland are next brought together, first with three or four mattress sutures through the substance of the gland, and then with a continuous suture on the surface. All bleeding points are carefully picked up and ligatured with fine catgut. The pretracheal muscles and the platysma are also carefully sutured, and the wound is closed with Michel's clips over a corrugated rubber drain. The drain is removed after 24 hours and the clips on the third day. The patient may be allowed up on the third day (figures 3 and 4, plate XXVI).

Hemithyroidectomy is performed in suspected cases of malignancy. My practice is to turn the gland over to the mid-line, and, having first ascertained the safety of the recurrent laryngeal nerve, to cut through the isthmus. I have stated before that adenomata arising from the isthmus itself are, I find, more difficult. They are not as easy to get round, and they have a blood supply from both sides. This increases the danger of hæmorrhage. Often they are most difficult to dissect off the underlying trachea.

Cystic tumours, if single, are often easily dissected out of the main gland substance. If they are small and numerous, then partial thyroidectomy is the better procedure.

In non-toxic nodular and cystic goitres, out of a series of 65 operations there has been 1 death, a mortality of approximately 2 per cent.

Individual operators have their own technique, and I am of the opinion that they achieve best results with their own methods. For anaesthesia some prefer to use local anaesthesia always; others use colonic olive oil and ether. There are operators who use the Crile method, cutting through the thyroid isthmus in the mid-line and then reflecting the gland outwards. There are others who practise actual section of the gland without prior ligature of the superior and inferior thyroid vessels. They merely place forceps all around the gland on the vessels and then do a wedge-shaped excision (figure 1, plate XXVI). Whatever the procedure adopted, there is one undeniable fact; the surgery of goitre, though perhaps more delicate, is no more dangerous or hæmorrhagic than that on most other parts of the human anatomy.

I am grateful to the Agency Surgeon, Gilgit, for giving me permission to write this article.

VITAMIN A AND NIGHT VISION

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NIGHT-BLINDNESS was attributed to scurvy by Capt. Cook, even though it failed to clear up like other scorbutic symptoms when the

patient got fresh lemons. Bamfield noted in 1814 that fresh meat and vegetables, added to the diet, improved night vision, whereas anti-scorbutics did not; yet he too regarded it as a manifestation of scurvy. The full picture of vitamin A deficiency, as it affects the eyes, was observed by Holmes-Spicer in 1893. During the war of 1914-1918, Birch-Hirschfeld (1917) specifically mentioned a certain deficiency as the possible cause of the great increase in night-blindness in the German Army during the winter of 1916. Bloch (1921) attributed the outbreak of xerophthalmia in Denmark in 1917 to a deficiency of fat-soluble vitamin, and the epidemic subsided immediately rationed butter at a controlled price became available to the population. Finally, Wald in 1941 demonstrated the part played by vitamin A in the light-dark circle of visual purple, and the real importance of vitamin A in the process of night vision was fully established. In war time, and especially in the forward areas where diet is not all that is desirable, and the black-out is enforced, vitamin A should play an important part in our lives. In the winter of 1943, I carried out this survey to ascertain whether the army suffered from sub-clinical vitamin A deficiency, and whether many of the complaints of night-blindness had an organic basis. Vitamin A deficiency may exhibit itself by gross pathological symptoms like xerosis, phrynoderma, etc., but before these gross pathological changes are manifested the person passes through a stage of sub-clinical deficiency wherein only functional changes take place. The most important functional change that can be quantitatively assayed is defective dark adaptation. It is known that the photo-sensitive principle of the retina, the visual purple, is a combination of protein, vitamin A, and some other biological compounds. When light reaches the retina, the visual purple is converted to visual yellow, and after a time-interval this visual yellow is reformed to visual purple. This time-interval is proved to be directly proportional to the vitamin A present in the organism. Therefore, the recovery time of the visual purple is made use of in assaying the vitamin A sub-nutrition of an individual by the instrument known as a bio-photometer. The instruments in use are Birch-Hirschfeld's photometer, Hacht's adaptometer, Jeans and Zentmire, Rowett's adaptometer. The instrument used in this survey is one devised by Prof. Sankaran at the Institute of Hygiene, Calcutta (see figure 1). It consists of an ordinary microscopic lamp (L) supplying the test source of illumination. There is an iris diaphragm (D), manipulated by a handle traversing a graduated scale; an opal glass diffuser (E), and a ground-glass screen (C). The test plate (A) is a quincunx, a metal plate with perforations at the four corners and in the centre of a square of calculated measurement.

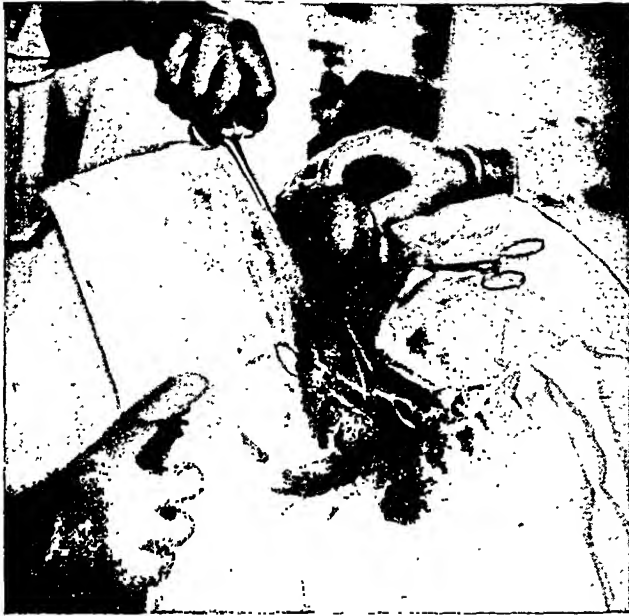


Fig. 1.—Artery forceps have been placed around the goitre prior to wedge-shaped excision.



Fig. 2.—A catgut ligature is being passed under the superior thyroid artery and it is about to be tied.



Fig. 3.—Before partial thyroidectomy.



Fig. 4.—Ten days after.

PLATE XXVII
VITAMIN A AND NIGHT VISION : N. U. KHAN. PAGE 608.

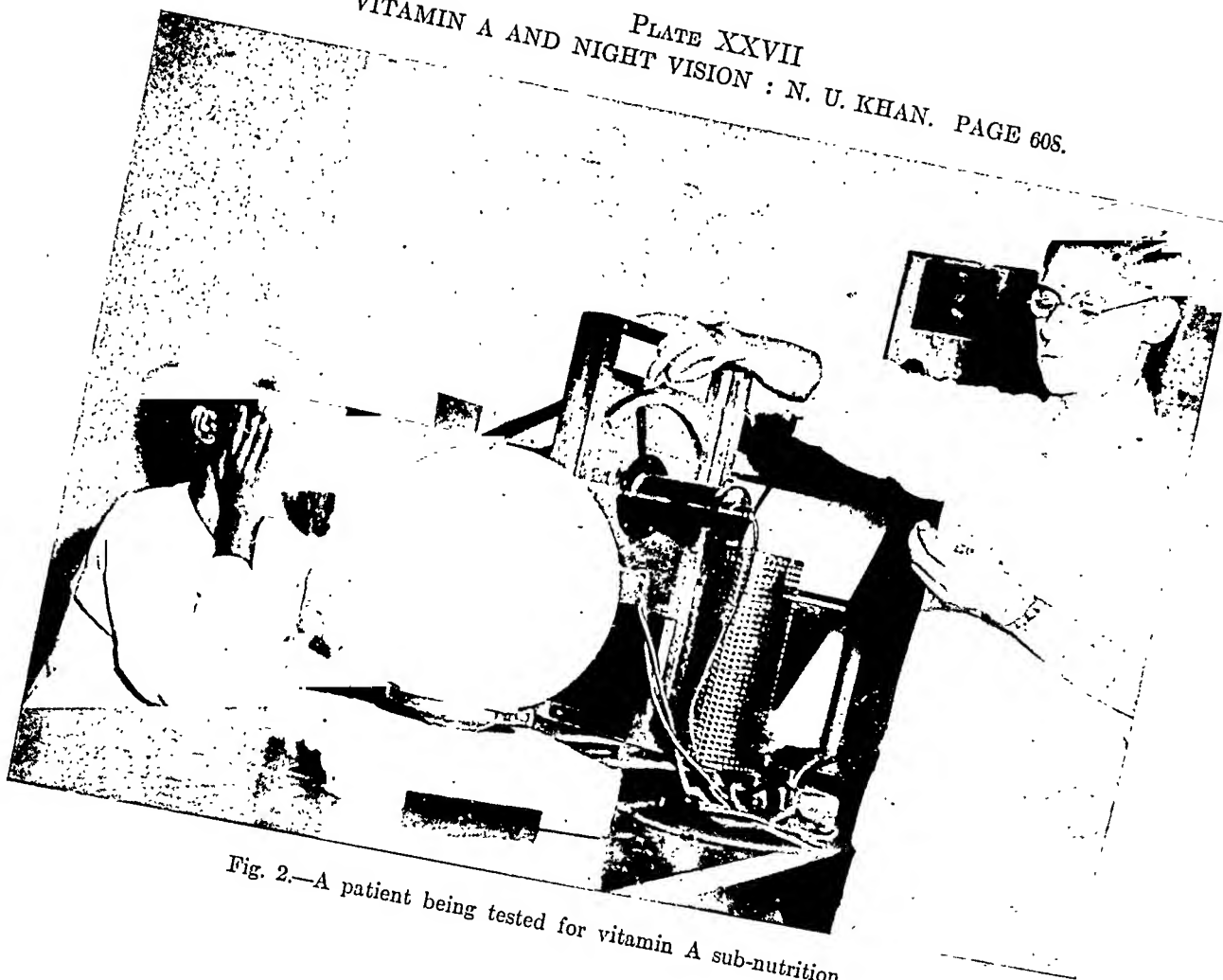


Fig. 2.—A patient being tested for vitamin A sub-nutrition.

A Goldberg wedge (B) is a glass plate completely opaque at one side, and completely transparent at the other, with intermediate gradations of light in between. The pointer on the handle of the iris diaphragm marks the gradation necessary for the patient to perceive the central dot of the quincunx.

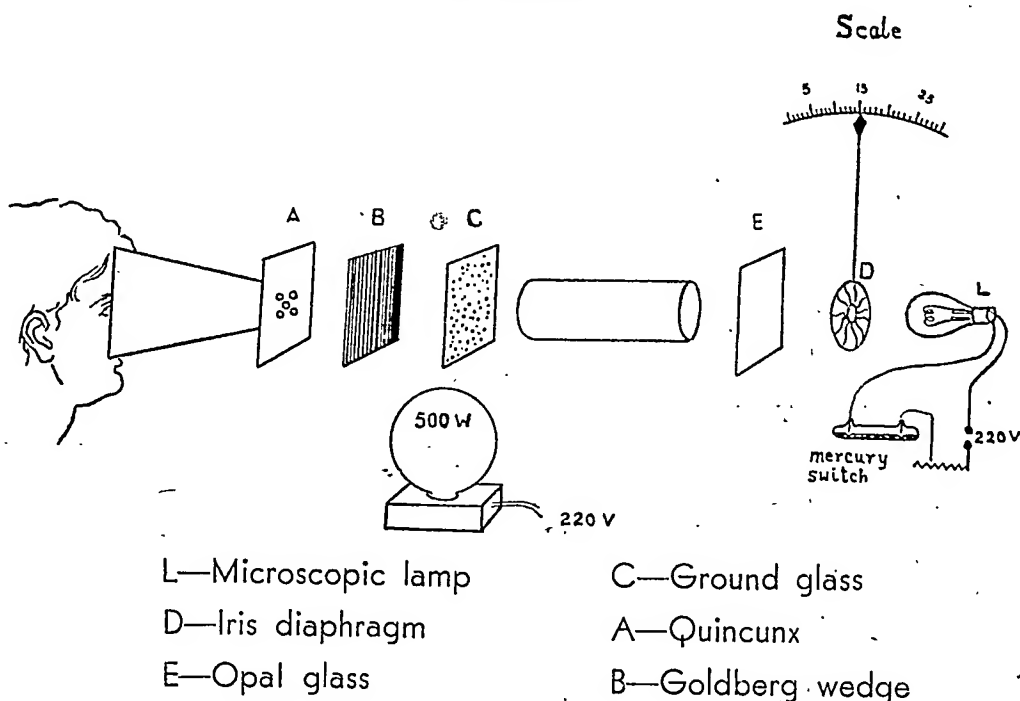
The examinations were carried out at night, but, if a dark room is available, the biophotometer can be used during the day. The patient is made to acquaint himself with the surroundings, and the process of testing. He is made to wait in the darkened room for 15 minutes for the visual purple to come to a state of equilibrium, so that the examination of the subse-

quent patients also is commenced when they have attained a similar adaptation of their retinae. Thus, all the results, having been taken under standard conditions, are comparable.

After the patient is conversant with the details of the test, he is made to look at the powerful source of light, the opal globe, for 30 seconds without closing his eyes (see figure 2, plate XXVII). While looking at this globe, if the individual happens to wear glasses with advanced errors of refraction, they are removed to avoid smarting of the eyes. The glasses have to be put on immediately the opal globe is put out, and he is asked to look into the view-finder. Then as soon as the subject finishes looking at the bright source of light, he is immediately asked to look into the photometric viewer, the light (L) is switched on, and the diaphragm is gradually opened till he is able to see the central dot of the quincunx. Value no. 1 gives a rough indication of his deficiency and also gives a reminder to the patient of the exact location of the central dot which he has to look for subsequently. Then the light (L) is put off, and the reading is taken on the diaphragm dial (D) seen with a small pocket torch, and the shutter completely closed. The patient is made to continue to look into the dark view-finder for 2½ minutes, during which time he is given a chance to reform the visual purple as much as his circulation can replenish the vitamin A. Immediately after 2½ minutes, (L) is lighted and

value no. 2 is taken when he is first able to perceive the central dot as the iris diaphragm is gradually opened. For this experiment, Sankaran found that a person, having the

Fig. 1.—Sankaran's instrument for assaying vitamin A sub-nutrition.



optimum reserve of vitamin A, has a value of 10 units of light for the first reading, and 4 units of light for the second reading.

Sankaran's biophotometer has the advantage over other instruments that (a) the time taken for a test on each person is less than 5 minutes, and a large number of examinations can be made at one sitting, and (b) the silent mercury switch of the light (L) gives an opportunity for the operator to check whether the patient is giving a sensible answer or not.

Results.—With this apparatus 1,280 members of His Majesty's forces were examined in a forward area. To test the accuracy of the instrument, 25 healthy medical officers of the hospital staff were examined; all of them gave normal readings. Then 15 female nurses, 50 British officer patients in the hospital, 100 British soldiers and 1,090 Indian soldiers were examined. None of these were selected but taken from the convalescent patients in the hospital, most of these were suffering from malaria. Out of 1,090 Indians, 280 were of the static unit who were not patients. They were specially included to find out whether malaria, which was by far the commonest malady of patients tested, could give any variation in vitamin A content or night vision; if anything, the hospital patients showed slightly better results than the Indian soldiers of that unit. Those patients who gave abnormal results were retested with

the photometer. In 50 consecutive abnormal cases, the retest showed no appreciable difference in the first repeat test—rarely over one unit. Those with defective adaptations were examined the following morning to discover if any organic eye changes were responsible for the poor dark vision, and if an organic cause was discovered, they were excluded from this survey. Of the 50 British officers, 5 (10 per cent) showed poor dark adaptation; of 100 British soldiers 14 (14 per cent), and out of 1,090 Indian soldiers 319 (29.2 per cent) were below par (*vide* table A). Amongst the British

dark; while 2 had normal dark adaptation; 8 showed moderate, 6 great, and 20 serious defect in dark adaptation.

Thus it appears that the complaint of night-blindness in the army is not common in its true form, though poor dark adaptation seems to suggest night-blindness to the patient (as in 30 of 32 Indian soldiers).

In the light of the Oxford Nutrition Survey, recent investigations by Stephens (1942) upon 10 male volunteers of normal nutrition, showed that dark adaptation of 8 of them became poor after a month of vitamin A deficient diet; but

TABLE A

Results of biophotometer examination of 1,280 military personnel

	Total	NORMAL		DEFECTIVE		5-10		11-15		16		Night-blind
		Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent	
Medical officers ..	25	25	100.0
British officers ..	50	45	90.0	5	10.0	5	10.0
British soldiers ..	100	86	86.0	14	14.0	14	14.0
Nurses ..	15	13	86.7	2	13.3	2	13.3
Indian soldiers ..	1,090	790	70.8	319	29.2	180	16.5	65	6.0	41	3.6	2
TOTAL ..	1,280	959	73.4	340	26.6	201	15.5	65	6.0	41	3.6	2

officers and men, none showed gross defects in night vision, but out of 319 Indian soldiers showing some defect 180 (16.5 per cent) showed moderate defect; 65 (6 per cent) considerable defect and 41 (3.6 per cent) severe defect. Two Indians could not see the centre dot at all.

38 (3.5 per cent) of the 1,090 Indians complained of night-blindness. Of this number, there were only 2 who could not see in the

after a single dose of halibut oil, the light threshold fell sharply, and after a few further doses the original level was reached. Twenty-five Indians with deficient vitamin A were treated with vitaminized oil, one ounce three times a day. After one week's treatment, all of them improved, and 18 showed normal dark adaptation. The rest, with the exception of one, reached normal limits after another week (*see* table B).

TABLE

Results of administration of vitaminized oil

No.	1	2	3	4	5	6	7	8	9	10	11	12
a	16/5	22/9	16/8	20/12	17/7	21/8	22/8	28/11	30/9	17/6	25/12	12/10
b	8/4	6/4	10/4	11/6	12/5	12/7	8/4	9/4	26/9	9/3	20/9	8/4
c	8/4	8/3	9/4	20/9	..	10/4	..

a. Figures before treatment.

b. Figures one week after treatment.

The numbers represent units of light for the first Normal is 10/4.

Left figure is the first reading and the right figure

The term vitamin A covers two closely related substances (A₁ and A₂) functioning essentially as if they were one. These are colourless, fat soluble, and fairly stable substances which can withstand the ordinary process of cooking and heating. There are at least four substances (alpha, beta and gamma carotenes, and cryptoxanthin) known to be precursors of vitamin A. These vitamin A precursors are readily hydrolyzed in the body, chiefly in the liver, yielding vitamin A. Hence the presence of any of these precursors in the food adds to its vitamin A value, though not to its vitamin A content. Fish-liver oil contains vitamin A and practically none of its precursors; green leaves have a high vitamin A value, but no vitamin A; and animal organs often contain both vitamin A and some unchanged precursors, usually carotenes, and this is also true of milk and eggs. A molecule of beta carotene C₄₀H₅₆ yields two molecules of vitamin A₂ C₂₀H₃₀. This carotene molecule is symmetrical, and the link of hydrolysis is a double chain at the centre of the molecule, each half taking both the H and OH of a molecule of water. Beta carotene thus yields very slightly over its own weight of vitamin A. The other precursors also hydrolyze at a double link, but as their molecules are not symmetrical, each of them yields only one molecule of vitamin A. Thus each of the other three precursors has only one half as much vitamin A value as has beta carotene. The human body is capable of storing vitamin A in quantities sufficient to meet the nutrition needs for a considerable time. The quantity required by a human adult, as reported in 1939 by Booher, Callison and Newton, is 1,750-3,850 I. U. per day in the form of vitamin A; 3,010-7,210 I. U. in the form of carotene. In Booher's experiment on 5 'ostentatiously healthy' humans, the depletion period varied from 16 to 124 days. In 1937 the adult requirement for vitamin A was assessed by a Technical

Commission of the League of Nations at about 3,000 I. U. a day. It was suggested that this intake could be assured by taking a pint of milk, one egg, one ounce of butter and a helping of green vegetables daily. But this diet is rarely possible in war time, especially in the field. However, the gross carotene content of carrots, as estimated by chemical tests, is usually 2,200 to 4,000 I. U./100 grammes which means that even with inefficient absorption, carrots must be a valuable source of vitamin A.

Carotene is not destroyed by cooking, and there is evidence that cooking increases digestibility with a corresponding increase in the efficiency of absorption of carotene. Greens of the spinach type, and in India the common growing *saks*, are rich sources of vitamin A, as also several other Indian vegetables (see table C). The preservation of these vegetables can provide a cheap and rich source of vitamin A. For example the Indian dishes prepared from carrots—halva, muraba, gagrale, etc.—can be easily preserved and transported even to the front line.

Summary and conclusion

An account is given of a study of dark adaptation of 1,280 army personnel. 14 per cent of British soldiers and 29.2 per cent of Indian soldiers showed defective dark adaptation as tested by Sankaran's photometer. Twenty-six of the Indians with defective vision were treated with vitaminized oil. All, except one, developed normal dark adaptation within two weeks. Thirty-six (3.2 per cent) of the Indians complained of night-blindness, but only two of them were night-blind, though 28 of them showed defective dark vision. A discussion of the application of recent knowledge of vitamin A to war-time nutrition in India is given, and it is suggested that greater use should be made of foodstuffs, such as carrots and *saks*, which are plentiful in India, and are a rich source of vitamin A.

B
to patients with vitamin A deficiency

13	14	15	16	17	18	19	20	21	22	23	24	25
17/8	20/14	17/7	20/11	15/6	15/8	16/8	12/6	13/5	16/9	11/9	16/10	13/6
7/4	16/10	8/4	12/8	9/4	8/3	9/4	6/3	8/3	9/3	9/4	9/4	8/3
..	9/4	..	8/3

c. Figures two weeks after treatment.
and second readings.

the second reading.

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TABLE C
Vitamin A content of some common Indian
saks and other articles of food

Foods	I.U./100 grammes
Belati begun (tomato)	35,640
Dala sak	25,200
Dhanne sak	12,630
Mango	11,790
Drum stick	6,798
Palang sak	6,500
Kalmi sak	5,500
Pudina sak	4,600
Methi sak	4,500
Milk	3,500-5,000
Butter	3,500-5,000
Sulpa sak	3,200
Ladies' fingers	2,318
Spinach	1,378
Papaya, ripe	1,212-1,500
Carrots	1,140
Eggs	1,000-2,000

My most grateful thanks are due to Prof. G. Sankaran, who loaned me his photometer. Without this loan, this study would have been impossible. I am also indebted to Colonel C. R. Henderson, I.A.M.C., Commanding Officer, and to Lieut.-Colonel M. H. Shah, O.C., Medical Division, for their encouragement and permission to carry out this study and Brigadier S. W. Ian Hill, Consulting Physician, for his criticism and help in preparing this paper.
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ULTRA-VIOLET THERAPY IN CASES OF LEUCODERMA

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In this short paper I shall only attempt to discuss the place of ultra-violet ray therapy in the treatment of cases of leucoderma or vitiligo as noticed in the actinotherapy section of the Radiology Department of the Stanley Hospital, Madras. Before proceeding to discuss the effect of ultra-violet rays on conditions in which there is an absence of normal pigment in the skin, it will be advantageous to state briefly the known facts about normal pigmentation in the skin and the effect of ultra-violet rays on normal skin.

The normal skin is from 0.5 to 10 millimetres thick, varying from place to place in the body, and consists of two layers, the epidermis and the dermis. The more superficial layer of the skin is the avascular epidermis which consists of stratified epithelium accurately

moulded on the papillae of the corium or true skin. The lowest or the deepest layer of the epidermis is known as the basal layer, palisade layer or stratum germinativum. It is made up of columnar cells placed close together and containing a quantity of pigment, the amount varying with the colour of the individual.

The physiological pigmentation of the skin is produced by a corpuscular organic pigment 'melanin', varying from pale yellow to deep black. It is distinguished from blood pigment by being iron-free. Almost all the pigment is contained in the cytoplasm of the various cells. Some of these cells, called melanoblasts, have made this pigment, while others, called melanophores, have only taken up the pigment granules are normally seen in the basal layers of the epidermis as a small dome above the nuclei of the cells, in the corresponding portion of the hair follicle, and in the hairs themselves. This pigment is formed by the oxidation of a colourless mother-substance, the oxidation being activated by a ferment (Goldsmith).

Raper, using tyrosinase in the meal worm, found that:—Tyrosin + tyrosinase + oxygen → 3 : 4 dihydroxy-phenylalanin (dopa). Using dopa as his melanogen, and employing skin sections instead of extracts, Bloch has elaborated the very important dopa reaction.

Dopa reaction.—Frozen sections of fresh skin are immersed in a 1 in 1,000 watery solution of dopa with pH value of 7.3 to 7.4 and later washed in distilled water. It is then observed that certain cells are coloured, the colour varying from grey to black. These cells must therefore have contained a ferment which has converted the dopa into melanin. This change occurs exclusively in the cytoplasm, and the ferment is referred to as dopa oxidase. This reaction is found to be negative in the case of skin from albinos, scars and leucoderma patches, while it is found to be intensified in those cases where the human skin shows a tendency to hyperpigmentation after irradiation with ultra-violet rays. In the human skin, the dopa reaction is positive in the cells of the basal layer of the epidermis and hair follicles, which are therefore called melanoblasts. In the spindle cells of the corium, though there are some pigment granules, the reaction is negative, and since they only carry pigment granules which have escaped from the basal layer, they are called melanophores.

There are many theories regarding the origin of the pigment in the skin, but to me only two appear to be reasonable and probable.

A. Bloch's theory is that both pigment and adrenalin have a common forerunner—mother-substance—in the general circulation which is generated by melanoblasts of the skin as well as to the suprarenals by circulation. Melanoblasts, with the aid of an oxidase ferment, convert pro-pigment into melanin pigment in the skin, while the suprarenals convert it (pro-pigment) into adrenalin.

B. Murosky and others state that the pigment mother-substance originates in the melanoblasts themselves, and that, after expulsion from within the nucleus, it is transformed into melanin in the protoplasm of the cells.

One of the chief direct effects on skin as a result of exposure to ultra-violet rays is pigmentation. Sometimes it is produced without any erythema being noticed. Ultra-violet rays with wave-lengths ranging between 3,000 A.U. and 2,800 A.U. are believed to produce the pigment in the basal cells. Even though the ultra-violet ray is the chief producer of pigment in the skin, it is not the sole producer, as pigmentation is also produced by the repeated stimulation of the skin by certain agents. All persons do not get the same benefit from exposure to ultra-violet rays. To quote Lee



Fig. 1.—Case 1. Before treatment.



Fig. 2.—Case 1. After treatment.



Fig. 3.—Case 2. Left side. Before treatment.



Fig. 4.—Case 2. Left side. After treatment.



Fig. 5.—Case 2. Right side. Before treatment.



Fig. 6.—Case 2. Right side. After treatment.



Fig. 7.—Photomicrograph of skin clipping from case 3 ($\times 250$). Before treatment.



Fig. 8.—Photomicrograph of skin clipping from case 3 ($\times 250$). After treatment.



Fig. 9.—Case 3. Before treatment.



Fig. 10.—Case 3. After treatment.



Fig. 11.—Case 3. Before treatment.



Fig. 12.—Case 3. After treatment.

Macarthy 'Every individual is born with a varying susceptibility to light, and therefore responds differently in the production of pigment. Examples of this are the response to light offered by blondes and brunettes and those unhappy individuals who develop xeroderma pigmentosa'. The colour of the normal skin depends not only on its pigment content but also on its horny layer and blood content. In the normal skin, the capillary dilatation causes a reddening; but on the whole it is mainly the pigment content that regulates the colour of the skin.

Savill in his *System of Clinical Medicine* defines leucoderma (synonym—vitiligo) as 'a condition in which there is an absence of normal pigment in areas which are surrounded by darker coloured skin.' Both congenital and acquired conditions are included in this term. But some dermatologists like Goldsmith include congenital achromic fixed patches under the term leucoderma, and the progressive acquired patches under vitiligo. Personally, I prefer to include both the conditions under a common term leucoderma, but not leuco-melanoderma syphilitica.

The exact causative factor of this disease is not known. Perhaps it might be a metabolic process in which depigmentation is only a local sign, or it might be an endocrine derangement, or it might even be of a pure nervous origin, or a combination of two or more of these factors. Bloch sees in vitiligo a kind of exhaustion of a primarily weak cell function as measured by the dopa reaction.

From September 1942, four cases of leucoderma underwent a full course (of six series) of ultra-violet ray exposures in the actino-therapeutic section of the Radiology Department, Stanley Hospital. Besides these, five other cases also attended the department for treatment, but as they had treatment for only a week or less they are not included in this review. The ultra-violet lamp used is the modern high-pressure mercury-arc alpine-sun quartz lamp in which there is a constant output.

Treatment.—Exposures were made at a distance of one metre, that is about 30 inches from the reflector edge of the ultra-violet ray lamp. According to the manufacturer, the distribution of the rays over the body of the patient is uniform at a distance of 30 inches from the reflector edge of the lamp (variations above or below the mean intensity being within 5 per cent). The minimum perceptible erythema dose is taken as the unit. (Generally, it is about three minutes' exposure at the standard distance of 30 inches.) The bare diseased area was therefore exposed to the rays, the part being kept at the standard distance of 30 inches from the reflector edge of the lamp. The minimum perceptible erythema dose was given on the first day, and on each succeeding day the dosage was progressively increased by adding a minute's exposure every day till a maximum

dosage of 12 minutes' exposure was reached, when it was continued and a full course of 26 exposures were given. The patient was then given a rest for two weeks and a fresh course was started. Thus a series of courses were given but those that did not show any improvement after six courses were considered as failures.

Clinical photographs were taken before, during and after treatment; examinations of blood and urine, and of all the systems were done as a routine measure in all the cases. In one case, skin clippings for pathological report were taken from the diseased area both before and after treatment. Out of the four cases of leucoderma that went through a full course of ultra-violet ray therapy, three showed definite and considerable improvement, and could almost be considered as cured, while the fourth with a leucodermic patch in the lower lip showed no appreciable improvement.

The following three cases showed definite and considerable improvement in their condition after ultra-violet ray therapy. Their clinical photographs taken before and after treatment are appended herewith (see plates XXVIII and XXIX).

Case 1.—A well-nourished boy of 14 years, showing no abnormality of any kind apart from the skin condition, attended on 4th September, 1942. The skin condition was of one year's duration. Fairly wide areas of depigmentation with irregular edges were found on the anterior aspect of both legs below the knees. A few small patches on the foot and a few spots on the face and forearm were also noticed. There was no loss of sensation over these depigmented areas.

The first course of ultra-violet ray exposures over the diseased parts was completed on 5th October, 1942, and on examination, a few pigmented spots were noticed on the original depigmented areas. The treatment was continued. On 16th February, 1943, pigmented islets were found to have enlarged with some of them coalescing. Five weeks later depigmented spots on the face were replaced by normally pigmented skin, and the pigmented islets on the leg and forearm were considerably enlarged. After another three months the skin appeared to be normal except for a few depigmented spots on legs and foot.

Case 2.—A girl, aged 15 years, in good general condition, came on 9th February, 1945, for the treatment of leucoderma. A small depigmented patch had started on the right lateral aspect of the abdomen, and later another small spot on the left lateral border. These patches slowly grew to their present dimensions. A depigmented patch about $4 \times 1\frac{1}{2}$ inches roughly quadrilateral in shape was situated on the infero-lateral border of the abdomen on the right side extending posteriorly; another similar patch about $2\frac{1}{2} \times 1$ inches on the left side also extending posteriorly. There was no loss of sensation over the depigmented areas.

On the 25th day of ultra-violet ray treatment, a few pigmented islets were found in the depigmented areas. After three months of treatment the pigmented islets spread considerably and coalesced together so that a good portion of the original leucodermic patches was replaced by normal skin (see photograph). Unfortunately, a week later her father was transferred out of Madras and the patient had to forego further treatment.

Case 3.—A well-nourished woman of 22 years came for the treatment of leucoderma. Two years ago two depigmented spots started in the infero-lateral border of the abdomen on both sides, which later began to spread towards the back. A month and a half later

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depigmented areas also appeared on the legs. On examination, irregular depigmented areas were seen on the anterior aspect of both legs and on both inferolateral borders of the abdomen above the crests of the ileum, and also on the elbows. There was no loss of sensation over the patches. A skin clipping from the depigmented patch was sent for pathological examination and the report was: 'Epidermis is atrophic with absence of pigment cells. There are no sweat or sebaceous glands'.

After treatment for a month and a half, pigmented islets began to appear on the patches in the leg, and after four months on the abdominal patches also. A skin clipping from one of the pigmented islets on the leg was sent for pathological examination and the report was: 'Basal layers of the skin show pigmentation' (see photographs). The treatment is still being continued.

Conclusion

Ultra-violet ray therapy has a definite place in the treatment of leucoderma. Individual susceptibility does play a part in determining the extent or degree of cure. Particularly to those who are susceptible, energetic treatment by ultra-violet rays produces restoration of pigment in the leucodermic patches and I believe with permanent results. Those whose normal skin gets pigmented readily after exposure to ultra-violet rays are the people who show the best of results in treatment. In these cases, while the pigment in normal skin is increased, after a series of exposures to ultra-violet rays, in leucodermic patches pigment is restored. The 'dopa' reaction is negative in leucodermic skin, but it is positive in the pigmented area which has appeared subsequent to the exposure to ultra-violet rays.

If we accept the theory put forward by Bloch that the pigment-mother-substance—314 dioxyphenylalanin—is carried to the melanoblasts (basal cells) by the circulatory system, the ultra-violet rays by stimulating the melanoblasts produces the ferment dopa oxydase, which acting on the pro-pigment restores the pigment in leucodermic patch.

I take this opportunity to convey my grateful thanks to Dr. M. G. Kini, M.C., F.R.C.S., Supdt., Stanley Hospital, for the kind encouragement and help that he has given me, to Dr. K. C. Nambiar, F.R.C.S., Hon. Surgeon, Stanley Hospital, for taking the skin clippings, to the Professor of Pathology, Stanley Medical College, for examining and reporting on the skin sections and finally to my staff in the Radiology Department for their co-operation.

THE RELATION OF ARTERIAL BLOOD PRESSURE TO SUCCESSIVE PREGNANCIES AMONG A RURAL POPULATION IN CEYLON

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The present study was undertaken to ascertain the influence of successive pregnancies on arterial

blood pressure. The investigation was carried out in a hospital in the 'low country' of Ceylon, the inmates of which were chiefly composed of people from the rural areas. The occupation of the women in these areas is chiefly agricultural (paddy and *chena* cultivation, and tapping of rubber). Their resources are very few, most of them being daily wage earners. Their diet is mainly vegetarian, though a few have sufficient means to eat fish and meat about four times a month.

Blood pressures of 247 consecutive cases of expectant mothers in the last three months of pregnancy between the ages of 16 and 45 were recorded. The blood pressure in each case was estimated by the author, using the auscultatory method in the arm, with the patient in the recumbent position, as advocated by Hutchison and Hunter (1940). A comparison was made between the mean blood pressure of primigravidae and multigravidae in various age groups (table I).

TABLE I

	Age group	Number of cases	Mean systolic pressure	Mean diastolic pressure
Primigravidae	15-19	14	120	71
Multigravidae	15-19	6	122	73
Primigravidae	20-24	43	121	74
Multigravidae	20-24	41	115	64
Primigravidae	25-29	8	118	76
Multigravidae	25-29	52	115	72
Primigravidae	30-34	7	126	83
Multigravidae	30-34	48	119	72
Primigravidae	35-39	2	125	75
Multigravidae	35-39	18	121	70
Primigravidae	Above 40	8	116	60

It will be seen from table I that such a comparison is possible only in the age group 20 to 24, where there is an almost equal number of primigravidae and multigravidae. In this age group, the blood pressure both, systolic and diastolic, of primigravidae was higher than that of multigravidae. No such comparison was possible in the remaining age groups, as in the earlier age period, viz 15 to 19 years, there were more primigravidae and in the later age groups a larger number of multigravidae.

To study the effect of successive pregnancies on the blood pressure, the patients were divided into two groups: (a) first and second pregnancies, and (b) subsequent pregnancies, viz 3rd to 10th (table II).

TABLE II

	Number of cases	Mean systolic pressure	Mean diastolic pressure
Group (a)—1st and 2nd pregnancies.	121	120	72
Group (b)—3rd to 10th pregnancies.	126	117	70

No appreciable difference was noticed in the two groups. However the mean blood pressure was actually found to be lower in women who had passed through several pregnancies.

The incidence of hypertension in the two groups was then determined. Although different opinions have been expressed by various authors regarding the normal blood pressure, it is generally accepted that the blood pressure in tropical women is lower than that in European females. Chopra *et al.* (1942), in a large series of observations in non-pregnant women, state that the average systolic and diastolic pressures in Indian females on a mixed diet is 115.4 and 70.2 respectively. Thiagarajah (1941, 1943) is of the opinion that blood pressure over 120/80 constitutes hypertension, as he found that in a series of 159 cases of pre-eclampsia investigated by him in Ceylon, in only three cases was the blood pressure below this figure. In this study, any pressure which reached or exceeded 120/80 has been considered to constitute a hypertensive state. The incidence of hypertension in the two groups calculated according to this criterion is as follows (table III).

TABLE III

	Total number of cases	Number of cases of hypertension	Percentage
Group (a)—1st and 2nd pregnancies.	121	68	56.2
Group (b)—3rd to 10th pregnancies.	126	72	55.6

No appreciable difference in the incidence of hypertension in the two groups is noticed. The ages in group (a) ranged from 15 to 33 years, the average age being 23.4 years. In group (b) the ages ranged from 22 to 45 years, the average age being 30.1 years. Thus in group (b) are to be found not only cases of multiple pregnancies (three and over) but also more elderly women than those in group (a). In spite of both these differences, *viz* parity and age, a slightly larger proportion of women in their first and second pregnancies developed hypertension.

Discussion

It will be seen from table I that in the age group 20 to 24 the mean systolic pressure of primigravidae exceeded that of multigravidae by 6 mm. Hg, and the mean diastolic pressure by 10 mm. Hg. Table II shows that the effect of successive pregnancies, if any, is to reduce the blood pressure, for the mean systolic pressure of women in the 3rd to the 10th pregnancy was lower than that of women in the 1st and 2nd pregnancies by 3 mm. Hg. and the mean diastolic by 2 mm. Hg. The ultimate effect of successive pregnancies on blood pressure, if any, appears

to be salutary. Although it is thought that child-bearing throws a strain on the vascular system, which increases with each succeeding pregnancy, this is not shown to be the case with regard to blood pressure. There is no indication in this study that elevation of the blood pressure is caused by child-bearing.

The other important consideration is the effect of pregnancy on the incidence of hypertension. It was observed (*vide* table III) that the incidence of hypertension was slightly greater in the first two pregnancies than in subsequent ones. Hypertension is regarded to be an early physical sign of pre-eclamptic toxæmia. It is indeed of greater reliability to us in the tropics than albuminuria and oedema, because the two latter symptoms can be caused by more prevalent conditions like anæmia, malaria, ankylostomiasis, and malnutrition. Accepting the sign of hypertension as indicative of pre-eclamptic toxæmia, these studies show that the number of toxæmic (pre-eclamptic) cases was slightly greater in the earlier pregnancies than in later ones. Hence the liability to toxæmia does not depend on the number of pregnancies.

If the hypertension and consequently toxæmia of pregnancy are due to a renal factor as the result of damage to the kidneys caused by repeated child-births, the incidence of these conditions would be expected to rise with successive pregnancies. We find however that the incidence of hypertension is actually less in women who have borne several children, even in spite of their average age being 13 years more than that of women in the first two pregnancies. It is, therefore, reasonable to presume that hypertension and toxæmia have been caused by some unknown factor operating mainly in the earlier pregnancies.

Summary and conclusion

1. The systolic and diastolic blood pressures have been determined in 247 women who were admitted to a rural hospital in Ceylon in the last three months of pregnancy.
2. In the age group 20 to 24 years, the mean systolic and diastolic pressures were lower in multigravidae than in primigravidae.
3. The incidence of hypertension and consequently of toxæmia (pre-eclampsia) was lower in women with several children than in those with one child, in spite of the higher average age in the former group.
4. Thus a succession of pregnancies neither elevates the blood pressure nor causes a rise in the incidence of toxæmia. On the contrary both blood pressure and incidence of toxæmia tend to be lower in women who have undergone successive pregnancies.
5. It is argued that renal damage is not the causative agent of hypertension and toxæmia. An unknown factor which operates in the earlier pregnancies is the probable cause of these abnormal conditions.

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EOSINOPHILIA AND SOME PÉCULIARLY STAINING LEUCOCYTES

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Introduction.—'Eosinophilia' is very much in fashion just now in medical literature. Terms such as 'eosinophilia of lungs', 'tropical eosinophilia' and 'idiopathic eosinophilia' do certainly connote certain syndromes the existence of which cannot be denied. However, experience with certain peculiarly staining leucocytes met with under varying conditions of health may prove interesting in this connection, and this paper describes some practical difficulties and fallacies in the diagnosis of 'eosinophilia'.

The problem.—Differentiation of neutrophil polymorphonuclear leucocytes (polymorphs) from eosinophil polymorphonuclear leucocytes (eosinophils) is a comparatively easy matter, and yet cases have been seen both in India and in the Middle East where difficulties arose, the reason for the difficulty being a peculiar staining of some of the cells of the granulocyte series.

In all, 12 cases were studied, but only four are described showing clinical extremes. The peculiar cell is for convenience called the T cell. It is a polymorphonuclear leucocyte with eosinophil cytoplasm showing fine granules, the fineness in some instances being of ground-glass consistency. It shows a similarity to a polymorph in the nuclear pattern, and a similarity to an eosinophil in having acidophilic glass consistency to the typical coarse eosinophil granules. There is no leukemoid reaction. In warm-stage preparations, the polymorphonuclear cells are of two types: (a) cells with agranular or very finely granular cytoplasm, and (b) cells with coarse cytoplasm. The proportion of (a) to (b) varies from 1:2 to 3:1. The nucleus either has a cleft or is divided into two or three lobes, rarely into four; the spectacle-like appearance of the nucleus of the typical eosinophil is absent. The T cell is a

complete cell with a complete outline, and it is in the staining of the cytoplasm, including the granules, that the confusion in identification occurs.

Several series of slides were stained by Leishman's, Giemsa's, and mixed Leishman-Giemsa stains, the slides being washed with water of pH 6.8, 7.0, 7.2 and 7.4. While the slide as a whole showed the effect of the change of pH, the T cell could still be distinguished from the typical polymorph and eosinophil. In a number of instances, the T cell was found in the same microscopical field as other leucocytes, and it was often difficult to know exactly what to call the cell, a polymorph because of the polymorphonuclear nucleus, or an eosinophil because of the eosinophilic staining of the cytoplasm. The presence of a typical polymorph, a typical eosinophil, and a T cell side by side made this doubt very real. In a few instances the nucleus and the granules were like those of a polymorph, and yet the cytoplasm was distinctly acidophilic.

A number of slides were shown to a group of pathologists at Cairo in 1943: the T cell caused much confusion in differential counts on the same slides done by experienced pathologists. Two examples are quoted:—

Pathologist	A	B	C	D	E
<i>Slide 1</i>					
Neutrophils	33	72	36	67	56
Eosinophils	52	12	46	18	4
Lymphocytes	15	14	17	15	16
Monocytes	0	2	1	0	2
T cells	0	0	0	0	22
<i>Slide 2</i>					
Neutrophils	28	52	48	82	52
Eosinophils	62	40	40	2	1
Lymphocytes	9	8	12	15	12
Monocytes	1	0	0	1	1
T cells	0	0	0	0	34

In each case E represents the average of three counts done by ourselves and our technical staff; A, B, C and D did not concede that T cells should be classed separately. Slides were sent to other places and equally divergent results were obtained. It is quite obvious that on the same slide a diagnosis of normal, eosinophilia, and neutrophilia would be given. The acceptance of the T cell at least keeps the neutrophil and the eosinophil in their correct places.

One of the pathologists considered the staining unreliable; this was an invalid argument, because our laboratory was dealing with 70 to 80 slides daily and the staining was quite up to standard. Even if the staining was indifferent, it would not explain defective staining of some of the granulocytes only while others in the same field were correctly stained. Further, control staining in parallel ruled out errors in technique.

Case reports

Case 1.—A South Indian, aged 27, a strict vegetarian, complained of anorexia, fever, and pain in right hypochondrium for two weeks. Leucocytes were 11,000 per c.mm. with 75 per cent neutrophils and 2 per cent eosinophils. Treated with emetine with some improvement; later developed passive congestion of the right lung. Two months later while apparently considerably improved, the patient became febrile with generalized dull pain in the abdomen and severe pain in the right hypochondrium. Leucocytes were 23,000 per c.mm. with 89 per cent polymorphs of which 68 per cent were T cells, 8 per cent typical eosinophils, and the rest typical polymorphs. Congestion of the right lung was present but not sufficient to explain the hypochondriac pain. The patient died after two days. At autopsy the liver was found to be large and friable. There was marked eosinophilic infiltration in the liver, kidneys, and the spleen. Eosinophil leukaemia was a possible diagnosis, though the total leucocyte count was against it.

Case 2.—A North Indian, aged 32, a meat-eater, with general malaise followed in 4 or 5 days by coryza, headache, and low temperature. Leucocytes were 12,000 per c.mm. with 30 per cent of the polymorphonuclears being called T cells. Stool, urine and sputum normal. Blood normal except for leucocytosis which persisted for 4 to 5 weeks, the total count varying from 12 to 16 thousand, the polymorphonuclears amounting to 76 to 84 per cent; of these 30 to 42 per cent were T cells, and the rest typical neutrophils or eosinophils. After 6 weeks the counts were, total 7,400, and T cells 7 to 9 per cent. The diagnosis was 'common cold' and the patient was kept in hospital for this long period for investigation purposes only.

Case 3.—A normal looking soldier, aged 30, performing normal duties; he was under surveillance for syphilis. His haemoglobin was 13.4 grammes per cent; total leucocytes 9,100; there was a large proportion of T cells varying from 9 to 36 per cent during the four-month period he was under observation; finally he proved non-syphilitic.

Case 4.—A member of the laboratory staff, normal in every way. He showed 5 to 12 per cent of T cells for a period of 14 months, after which observations were discontinued.

Discussion.—Though it may be very questionable to consider these T cells as a separate class of leucocytes, it should be conceded that they are some atypical phases of granulocytes. Errors in diagnosis are certain to occur if they are merely grouped either with neutrophils or eosinophils according to no accepted principles. The plea is, therefore, made that they should tentatively be classed separately until agreement is obtained as to their nature. But what is their nature?

In leucocytosis due to *infection*, eosinophils are often crowded out by neutrophils; the persistence of eosinophils in this series partially excludes infection as a cause of the leucocytosis in these cases. The absence of myelocytes was noticeable, thus further excluding leucocytosis due to infection.

Schilling's *Jugend-formen*, generally taken as a sign of regeneration, were not a feature of the cases studied. Regeneration, if any, was therefore not more than of normal degree.

Peculiar staining or incomplete staining with vacuolation generally occurs in *degeneration*. There was no clinical evidence of toxæmia or any degenerative process at work, except

perhaps in the first case, nor was there any vacuolation of cytoplasm. Other signs of degeneration, such as the moth-eaten appearance of the edges of cells, or the bluish granules in the cytoplasm, were also absent.

The T cells do not necessarily indicate toxæmia for they have been seen in conditions other than toxæmia. The fact that they may also be found in health would suggest that they are perhaps effete cells, being occasionally present in health and markedly present in illness. The cells are undoubtedly leucocytes of the granulocyte series, and are for the present best considered as effete cells of the neutrophil series. There is more evidence for this than for calling them typical neutrophils, less so for considering them eosinophils. The peculiarity of staining is perhaps a measure of the degree of effeteness.

Eosinophilia has been inconstantly noted after emetine injections, but in the present series emetine was used in only one case.

Pathological leucocytes showing abnormality in size and variation of staining may result conceivably from a developmental anomaly and in conditions of disturbed hæmopoiesis, but there was no evidence of such conditions in the present cases.

Weingarten (1943) considers *tropical eosinophilia* as a separate entity, but lung signs described by him were not a feature in our series. The only similarity between his cases and ours appears to be the fact that most of the patients in both series lived near the sea, though not on the coast, for a year or two prior to the observations.

Characteristic cells with eosinophil cytoplasm infiltrating heart, liver, lungs and kidneys have been described by French and Weller (1942); these were considered to be the result of sulphonamide drugs, and were similar to our T cells. But this drug was not used in any of our cases.

Conclusion.—The divergence of opinion among pathologists should sound a warning against a facile diagnosis of eosinophilia. The eosinophil leucocyte is by definition a polymorphonuclear or a kidney-shaped nuclear cell with coarse acidophilic granules, and nothing else should be called an eosinophil. Strict adherence to such a definition would obviate any difficulty in differential leucocyte counts, even if T cells abound. It, therefore, becomes necessary to class them separately, fully allowing that they are neither typical neutrophils nor typical eosinophils; it would appear best to consider them as effete cells of the neutrophil series, found in health and more in illness.

Summary

1. The occurrence of certain peculiarly staining leucocytes is noted both in health and in sickness, and it is considered that they are effete cells of the neutrophil series.

2. A plea is made for classing them separately until agreement is reached as to their identity.

3. A warning is sounded against a facile diagnosis of eosinophilia.

4. Four cases are described where such cells have been studied, though the paper is based on 12 cases.

Postscript.—Since the above was written more instances of T cells have been seen. The identity of the cell would perhaps matter little if there was agreement as to their place in a differential count. It is feared that errors have already crept into literature owing to inclusion of these cells sometimes with neutrophils and at other times with eosinophils. The dictum that a cell is known by the company it keeps is fallacious here, because with a large proportion of T cells it is the company itself that becomes unrecognizable.

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ORDINARY WATER IN PLACE OF DISTILLED WATER IN SALINE TRANSFUSION IN CHOLERA

By S. K. SEN GUPTA

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C. P.*

DURING the recent severe cholera epidemic (June to September 1945) in a group of villages in the Central Provinces I, as medical officer-in-charge of the Mundi Hospital, had occasion to treat ninety-five cases by saline transfusion with a mortality of only four persons. Of these four deaths, one was due, in my opinion, to my not being able to give a second transfusion owing to the distance and pressure of work; the other three being due, in my opinion, to the patients having been given unsuitable food too soon.

I am convinced that the percentage of mortality in cases of moderate virulence, if properly treated by saline, should be very low, and in any case not more than 10 per cent. The usual difficulty in treating large number of cases in rural areas is the absence of sufficient stocks of distilled water. My supplies of distilled water were exhausted after I had treated only three cases, after which I had to work with sterilized and filtered ordinary well water. In not a single case was any untoward result noticed except an initial shivering which passed off after about fifteen minutes. On the other hand I am inclined to think that this shivering reaction had actually some beneficent effect on the patients in stopping the vomiting and purging earlier than those treated with distilled water. The usual Roger's hypertonic saline solutions with the addition of glucose (25 c.c., 25 per cent to each pint) was employed. No other drugs were employed except coramine in cases of obvious shock, and small doses of atropine sulphate in some cases complaining of

severe pain over the abdominal area, and excessive cramps.

Under these circumstances, I would suggest that other workers in the field should not be deterred by the non-availability of distilled water, but should give ordinary clean water a trial.

[*Note.*—For intravenous use, fresh pyrogen-free distilled water is of course highly desirable. In a cholera epidemic in rural areas, and often even in urban areas, fresh distilled pyrogen-free water is often unobtainable. Old distilled water, unless it has been stored in completely sealed and sterile containers, is often highly pyrogenic. Fresh undistilled water is often much better than doubtful old distilled water.

In the cholera wards in Calcutta hospitals, Calcutta tap water has usually been used, and while it gives rise to some febrile reactions, these are not usually very serious, and the results are usually good.

In rural areas, the editor has used fresh well water, filtered and boiled, with good results. He always teaches: 'In cholera give saline in the best water you have, but in case of necessity use well water, tap water or tank water rather than leave a patient collapsed from cholera without a transfusion'.—EDITOR, *I.M.G.J.*

GLYCERINE-SALINE FOR THE PRE- SERVATION OF DYSENTERIC STOOLS

A NOTE ON CONCENTRATION

By P. V. GHARPURE

MAJOR, I.M.S./I.A.M.C.

SACHS (1939) published an article, his summary of which is as follows:—

'It has been found that neutral glycerine-saline solution as prepared in military hospitals in this district is unsuitable.

The preparation of a buffered glycerine-saline solution containing an indicator is described. There has been an increase in the isolation of organisms belonging to the enteric, dysentery and cholera groups from specimens sent in this solution from out-stations. The solution has the advantage of being stable, and the presence of an indicator acts as a check on the suitability of the solution.

The undermentioned points relevant to specimens of faeces from dysentery cases have been discussed: (a) The age of fresh specimens; (b) the best type of specimen to be sent to the laboratory; (c) the most suitable method for selecting specimens.

Details of some improved methods of laboratory technique are given.'

Sachs gave his method of preparation of buffered glycerine-saline solution as follows:—

'To 1,000 cubic centimetres glycerine add 2,000 cubic centimetres saline solution.

To this mixture add sufficient phenol red solution to match the standard indicator (phenol red) tubes in the pH set.

Add sufficient Na_2PHO_4 solution to adjust reaction to pH 8.0.

Tube off in 10 cubic centimetres bulks in one ounce screw capped bottles.

Sterilize either fractionally or for ten minutes in the autoclave at ten pounds pressure.

The reaction after sterilization will be about pH 7.4.'

The results were rightly claimed to be superior to those claimed with the ordinary neutral glycerine-saline solution in isolating dysentery bacilli and, in some cases, salmonella. The new fluid was found to be more stable in its reaction.

Work was undertaken to study the best concentration of glycerine leaving all other characters of the solution unaltered. With the use of a mixture of *B. coli* and *B. flexneri* as test organisms and the original Sachs glycerine-saline, very interesting results were obtained.

The first plate showed both the organisms well; 24 hours later there was suspicion of reduction of *B. coli*. At the end of 48 hours, further reduction was noted, finally after the mixture was in the fluid for 96 hours and over there was no growth at all. Though these results were not uniform in all experiments, the findings were considered a sufficient evidence that long contact with a 30 per cent glycerine tended to reduce if not to completely kill pathogens. The method of collection in glycerine-saline is primarily advocated to enable distant stations to transport material to the laboratory for isolation. It is worth knowing that there may be situations where materials may not reach a laboratory in less than 5 days, and, if my findings have any value, the object of the method is defeated. It was on this account that I undertook the study of the glycerine concentration which can preserve pathogenic bacteria of the dysentery group longer.

The following percentages of glycerine were used: 15, 12, 9, 6 and 3. Throughout the work, purest double distilled glycerine was used. Preliminary tests were carried out with a mixture of *B. coli* and *B. flexneri*. The next series was done with the same mixture in an emulsion of fresh human stool preferably a diarrhoea stool. Without going into the small details, suffice to say that 12 per cent was found to be the best. The lower strengths allowed proliferation of the organisms, the reaction changed far too quickly, and results were considered entirely unsatisfactory.

It is possible that the range may be 10½ to 12 per cent glycerine. With a 10½ per cent glycerine-saline and using dysentery bacilli as inoculum, taking all sterile precautions at every examination, it was found that some bacilli survived for as long a period as 54 days. This requires repeating, as my statement is based on a single finding.

In addition to providing a more appropriate medium, a lower concentration will effect economy.

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A COPPER SULPHATE FLOTATION METHOD FOR THE EXAMINATION OF *E. HISTOLYTICA* CYSTS

By H. S. SINHA

MAJOR, I.M.S./I.A.M.C.

Officer Commanding, 28 Indian Field Laboratory

Introduction.—The examination of stools by direct method for *E. histolytica* cysts is one of

the most difficult problems in routine clinical pathological work. Various other methods have been tried, but so far none has proved satisfactory. The necessity for a quick and accurate method of finding *E. histolytica* cysts in stools cannot be overestimated.

The idea of a flotation method for the detection of *E. histolytica* cysts originated from that of finding ankylostoma ova in saturated solutions of common salt. A solution which would just allow the *E. histolytica* cysts to float on the surface is essential for this method. Although the *E. histolytica* cyst (7 to 12μ) is much smaller in size than the ankylostoma ova (40 to 60μ), its specific gravity is higher and hence it does not float in saturated common salt solutions. The red blood cells, which are of the same size (7 to 8μ) as the *E. histolytica* cysts, float in blood the specific gravity of which varies from 1050 to 1060. As the red cell contains hæmoglobin it is assumed to be heavier than the *E. histolytica* cyst, and hence the required solution to float the *E. histolytica* cyst must be of a specific gravity lower than 1056. It was thought that the series of bottles containing copper sulphate solution used for measuring the specific gravity of whole blood and serum in the copper sulphate method of Phillips, van Slyke and others, could be used to determine the range of specific gravity of copper sulphate solution at which the *E. histolytica* cyst will float.

PRELIMINARY WORK

Preparation of copper sulphate solutions

(Adopted from the booklet entitled 'Copper sulphate method for measuring specific gravities of whole blood and plasma' by Phillips, van Slyke, Dole *et al.*)

Place 2½ lb. of $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ in the form of fine crystals into a 2-litre bottle. Measure 1,250 c.cm. of distilled water at room temperature into the bottle. Stopper the bottle and shake vigorously by repeated inversion for 5 minutes. Set the bottle down, immediately insert a thermometer into the solution and record its temperature nearest to half degree centigrade. Decant the solution at once from the bottle into a prepared funnel leaving the bulk of the crystals behind in the bottle. Complete the filtration as quickly as possible, keeping the funnel filled with the solution until all of the liquid above the crystals has been emptied out of the bottle.

From this saturated solution, measure into a 500 c.cm. cylinder the volume of solution indicated in the table below for the temperature of the saturation point of the copper sulphate solution previously recorded. Pour the entire solution thus measured from the 500 c.cm. cylinder into a 1-litre volumetric flask, and drain for two minutes to complete the transfer. Then fill the flask to the mark with distilled water and invert 10 times to mix the solution.

Volume of saturated copper sulphate solution to dilute to one litre to prepare stock solution of $D_{20}^{20} = 1.000$.

Stand the flask upright. The mixing results in a shrinkage of volume, so that the meniscus falls below the mark. To correct this shrinkage, let the flask stand for one minute until the solution drains down from the neck and then add enough water to bring the meniscus back to the mark. Stopper the flask, again mix the solution and transfer to a 2-litre bottle for storage.

To prepare the standard specific gravity of 1035, measure 34 c.cm. of stock solution by a

burette into a 100 c.cm. volumetric flask and fill the flask with distilled water. Mix the solution, transfer to a labelled 100 c.cm. bottle and stopper to prevent evaporation. Standard specific gravities of the rest of the series are prepared similarly, the number of cubic centimetres of stock solution being one less than the last two figures of the specific gravity required.

Temperature of the saturated solution at the time of saturation in °C.	Volume of solution to dilute to one litre, c.cm.
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20.0	489
20.5	485
21.0	481
21.5	477
22.0	474
22.5	470
23.0	466
23.5	463
24.0	459
24.5	456
25.0	453
25.5	450
26.0	446
26.5	443
27.0	440
27.5	438
28.0	435
28.5	432
29.0	429
29.5	427
30.0	424
30.5	421
31.0	418
31.5	415
32.0	412
32.5	410
33.0	407
33.5	404
34.0	401
34.5	398
35.0	395
35.5	392
36.0	389
36.5	387
37.0	384
37.5	381
38.0	378
38.5	374
39.0	371
39.5	368
40.0	365

A series of 50 c.cm. round bottles containing copper sulphate solutions of different specific gravities ranging from 1008 to 1050 was set up in a row and small cups* were placed in front of them. About 1 c.cm. of copper sulphate solution from each bottle was transferred to the respective cup in front. With a small coconut stick about 4 inches long, a pea-sized mass of stool positive for *E. histolytica* cyst was placed in each cup and emulsified thoroughly.

*Difficulties were experienced in finding suitable cups for flotation trials as big-sized cups would mean wasting large quantities of CuSO_4 solution. Metal caps of used penicillin bottles served the purpose well and were available in large amount. The capacity of each cup is about 3 c.cm.

The cups were then filled up with the copper sulphate solution from the corresponding bottles. Slides were placed on the cups lightly so that no air bubbles remained underneath the slide, and were kept for 10 minutes. Then, one end of the slide was held with two fingers of the left hand and the metal cup was pushed lightly with the coconut stick to the left side; at the same time the slide was turned upwards. As the metal cups are light, they stick to the slides and prevent the slides from being turned upward. The slides were examined with or without coverslips.

It was observed that when stools, especially of solid or semi-solid consistency, were put in CuSO_4 solution, a sticky mass was formed on the surface making the stool difficult to emulsify thoroughly; a proportion of the cysts became stuck in the stool and consequently the concentration was lowered. This difficulty was overcome by using 1 c.cm. normal saline to emulsify the inoculum and afterwards by filling up the cup (i.e. with 2 c.cm.) of CuSO_4 solution of specific gravity 1035, the specific gravity of the mixture thus becoming approximately 1015.

CuSO_4 solution, especially in higher specific gravities, has a tendency to form froth at the surface of the slides if the slides are allowed to stay on the cups for more than 10 minutes. This froth disperses cysts and makes it difficult to find them under the microscope. This froth can be broken up with a coconut or match stick or with the edge of the coverslip. Sometimes a fresh drop of CuSO_4 solution disperses the froth.

Slides from cups ranging in specific gravity from 1008 to 1023 showed a greater concentration of cysts and less faecal debris on the slides than those from cups of higher specific gravities. A series of tests was carried out to determine the exact specific gravity at which the concentration is maximum with the same stool, and the slides being kept for the same time (10 minutes). The higher the specific gravity of the solution beyond 1023, the more the faecal debris collected on the slides and the more difficult it became to find cysts.

Three sets of cups prepared in the above manner and containing copper sulphate solution ranging in density from 1008 to 1023 were arranged in three rows. Slides were kept for 5 minutes in the front row, for 10 minutes in the second row, and for 15 minutes in the back row and then examined. The slides from the first and second rows showed the maximum concentration and those from the back row showed too much froth, more faecal matter and apparently less concentration.

The technique as finally evolved

Apparatus and reagents required:—

CuSO_4 solution sp. gr. 1035	1 c.c. graduated pipette—1.
Normal saline	Dropping pipette with test—1.
Lugol's iodine	Metal cups, coconut sticks, etc.

Procedure

- (i) Place 1 c.c. normal saline in the cup.
- (ii) Pick up a specimen of the stool about the size of a pea with a coconut stick and place in the cup and emulsify with saline.
- (iii) Fill up the cup slowly to the brim with CuSO_4 solution (sp. gr. 1035) approximately 2 c.c.
- (iv) Cover the cup with a clean slide so that the slide is in direct contact with the fluid and there are no air bubbles between the slide and the emulsion.
- (v) Allow to stand for 10 minutes.
- (vi) Hold the nearer end of the slide with two fingers of left hand lightly and push the cup gently underneath the slide towards the left slide with the coconut stick and quickly turn the slide upwards.
- (vii) Examine the slide with or without a coverslip. The same slide can be examined with Lugol's iodine and this should be done immediately.

Comparison of the direct and the flotation methods

(i) *Relative concentration of cysts.*—Two specimens of stools heavily infected with *E. histolytica* cysts were obtained. Five slides were prepared from each of the specimens both by the direct method and by the flotation method and examined. The results are as follows:—

1st specimen—

Direct method—15 per 100 fields.

Flotation " —50 " " "

(sp. gr. 1015)

2nd specimen—

Direct method—10 " " "

Flotation " —40 " " "

(sp. gr. 1015)

(ii) *Detection of low-grade infection and of carriers.*—About 100 stools which were negative for *E. histolytica* cysts by the direct method were examined by the flotation method using solution of specific gravity 1015, and eleven showed the presence of *E. histolytica* cysts.

(iii) Even stools kept for 48 hours show cysts remarkably well by the flotation method, whereas the same stools examined by the direct method show blurred and cloudy cysts, perhaps due to the swelling of the keratinized covering. In the flotation method, the nuclei appear in bold relief, the chromatin membrane and nucleoli show very distinctly on a pale greenish background, very distinct dark chromatoid bars are seen. Differentiation from other cysts is very easy, and the concentration is much higher than by the direct method.

Summary

A flotation method with copper sulphate solution for the examination of *E. histolytica*

cysts in stools is described. The technique is simple and easy, and can be performed in any laboratory on a mass scale.

NOTES ON A SIMPLE TECHNIQUE OF SPLENIC CULTURE AT THE POST-MORTEM TABLE

By LEO KRAINER

MAJOR, R.A.M.C.

THE following technique has proved useful in the diagnosis of the enteric group of fevers and of septicæmia of various origin. The advantages are: increased probability of obtaining the organism, and adaptability to adverse circumstances, such as lack of facilities for heart-blood culture. Equipment: one or two throat swabs, one scalpel and one spirit burner.

Post mortem is to be carried out as soon after death as possible. Adequate sterilization of throat swabs is important.

Technique

The spleen is carefully exposed without exerting pressure, and then removed by dissection at the hilum. Care should be taken that no backflow of blood into the spleen is produced during dissection.

The surface of the spleen at the convexity is cleaned by wiping with dry cotton-wool, and then the capsule is heated with the spirit lamp in an area far from the hilum. The area of heating should be at least 5 cm. long.

The capsule is then incised without allowing the knife to enter the parenchyma. Subsequently the spleen is pressed apart in the area of the incision, so that the pulp appears, untouched by instrument or finger. (For that reason the method can be used without previous scalding.)

The throat swab is taken out of its tube, inserted into the pulp and rotated so that a fair amount of splenic tissue is attached to it, care being taken that the edges of the incision and the neighbouring pulp are not touched. Then the throat swab is replaced into its tube.

The throat swab is brought to the laboratory. A bottle of glucose-broth medium with a screw cap and a narrow neck—corresponding to the diameter of the test tube—is opened. The throat swab is inserted into the bottle so that its cotton-wool plug closes the opening. Alternatively the throat swab may be broken to the required length and inserted in the culture bottle, the latter being closed by the original screw cap.

The method was used in three instances and two controls.

Enteric group of fevers: *B. typhosum* isolated in pure culture (post mortem 4 hours after death).

Plague: *Pasteurella pestis* isolated in pure culture (post mortem 4 hours after death). Septicæmia following suppurative lesion of the big toe, the patient having been treated with sulpha drugs: *Staphylococcus aureus* in pure culture (post mortem 2 hours after death).

Controls.

Acute anterior poliomyelitis: Culture sterile after 48 hours (post mortem 7 hours after death).

Diphtheria: Culture sterile after 48 hours (post mortem 2 hours after death).

A Mirror of Hospital Practice

ACUTE INTUSSUSCEPTION DUE TO AN INVERTED MECKEL'S DIVERTICULUM

By MD. SIDDIQUILLAH KHAN, M.B., B.S.
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A girl, aged 12 years, was brought to the outpatient department on the morning of 3rd September, 1945, complaining of sudden abdominal pain, vomiting and constipation for the last two days. She was in acute pain, and was restless, her look was anxious and the abdomen was distended.

The patient gave a history of fever with rigors for six days. The fever came down every night with sweating. On the previous night she developed acute abdominal pain with vomiting; the vomitus did not contain blood or bile. The pain increased in intensity and radiated all over the abdomen, which became distended. She had not passed any faeces or flatus for two days. Her mother had noticed a lump to the right of the umbilicus.

On examination, the general condition of the patient was good, unlike what is usual in intussusception; pulse 160 with fair volume and tension; temperature 97°F. A sausage-shaped lump was prominent to the right of the umbilicus, with a concavity towards the umbilicus, and not moving on respiration. Waves of peristalsis were visible. On palpation, the lump was tender and hard, getting harder when a wave of peristalsis started. The lump could be moved to the left iliac region. No definite emptiness could be felt in the right iliac fossa. The lump was dull on percussion. Auscultation showed the presence of peristalsis. Examination per rectum showed no palpable mass and no blood on the examining finger. The spleen was palpable (two fingers). A diagnosis of intussusception was made. The blood slide showed benign tertian trophozoites in abundance and also gametocytes.

Immediate operation was decided upon. A soap and water enema was given and a few hard faecal masses were passed; as a result of this, the lump was much reduced in size and shifted to the left iliac fossa; the abdominal distension and the pain became less, but tenderness was present. At noon the abdomen was opened under general anaesthesia by a right paramedial incision. A little fluid was present. A coil of small intestine looking dusky, blue and oedematous caught the eye; this was exteriorized, and the diagnosis of intussusception was confirmed. Attempts at reduction were made, but proved futile, as all the layers of the intussusception were glued together, and the whole mass was so oedematous and friable that resection of the mass was decided upon. The two cut ends of the gut were closed separately, and a lateral anastomosis performed. Sulphathiazole powder was dusted in the abdomen which was then sutured in two layers. On dissecting the specimen, an inverted Meckel's diverticulum was found.

The convalescence was uneventful; the wound healed by first intention and the clips were removed nine days

after operation. The patient was given treatment for malaria. Her bowel function became normal and she was discharged a week later.

Comments.—According to Hamilton Bailey, Meckel's diverticulum is not an uncommon cause of intussusception at this unusual age. The absence of blood on rectal examination and the comparative absence of shock when compared with the common infantile form of intussusception are noteworthy features in this case.

My thanks are due to Major Charlewood, I.M.S., Civil Surgeon, Ajmer-Merwara, Ajmer, who performed the operation and gave me all facilities to follow up the case.

A TEAR IN THE WALL OF THE LARGE INTESTINE

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and

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Our only excuse for publishing the following case is the unusual nature of the accident and the very unusual injuries produced by it. On looking through the literature of the past several years, we have not come across any case published of a similar nature. The type of accident is not a rare one, but the injuries produced as reported in the literature have usually been perforations of the large intestine. In this particular case, as the case record will show, even with such a severe injury as that produced by an electrical air-compressor there was no perforation in the intestinal track.

A patient, Y. M., male, aged 35 years, was admitted in Sir J. J. Hospital as an emergency case at 3-10 p.m. on 14th April, 1945. He gave the following history:—

He was working in a squatting posture near an air-compressor machine in a factory, and was not aware that the nozzle of the air hose was lying near him. Another workman in the factory accidentally turned on the switch of the air-compressor machine, and the end of the air hose immediately started wriggling about, and accidentally came near the anal orifice of this workman. Air got pumped into his rectum, and the force of the jet was so great that he was suddenly thrown on the ground—face downwards. He immediately lost consciousness but came round in a few minutes. During this time the other workmen around him were laughing, thinking the whole affair to be a practical joke. But the patient looked ill and was taken to the factory dispensary. The doctor in charge did not suspect any severe injury and asked the patient to wait. The patient however soon began to feel giddy and could not sit up. He was therefore immediately sent to Sir J. J. Hospital.

On examination.—The patient was cold and clammy, restless and in severe pain. The respiratory rate was 60 and the respirations were shallow and as if difficult. The pulse rate was 120, with good volume, and regular.

The abdomen did not move well with respiration and was held rather rigid. The abdomen was tender all over and tympanitic around the umbilicus. The abdomen was silent, the liver dullness was obliterated but there was no free fluid detected in the abdomen.

On admission a turpentine enema was given with a good result. Turpentine stupes were applied to the abdomen and a flatus tube was passed every two hours.

Half hourly pulse, temperature and respiration records were kept. By 8 p.m. the pulse rate had increased markedly, the abdomen was still very resistant and there was a suspicion of free fluid in the abdomen. The patient was advised an operation but he refused.

The pulse rate was steadily increasing, with low volume. The patient's general condition had deteriorated but he did not consent to an operation till 4 a.m., 15th April, 1945.

The operation was done under spinal anaesthesia 1.5 c.cm. of 5 per cent stovaine (M.&B.) at 4 a.m.

On opening the abdomen there was no escape of gas, but the peritoneal cavity appeared to be full of fresh blood. A large number of clots were removed, before the intestines could be examined. The whole length of the small intestine from the duodeno-jejunal flexure right up to the ileo-colic sphincter was found to be normal. On examining the large bowel, however, there was found one almost continuous tear in the line of the anterior longitudinal band through serous and both muscular coats, but leaving the mucous membrane intact. The tear was continuous from a point where the rectum became intra-peritoneal right up to the caecum. The mucous membrane therefore appeared like one huge diverticulum. A flatus tube was passed up the rectum and the gas was allowed to escape. On each side of the line of the tear there were subserous hæmorrhages almost circular in shape, with a crenated margin. The average diameter of each patch was about $\frac{3}{4}$ of an inch. It was also noticed that from underneath the margins of the tear there was continuous oozing of blood. Suturing was started at the most distal end of the tear and was continued towards its proximal end. On reaching a point just short of the hepatic flexure, the patient suddenly collapsed. The abdomen was therefore closed in layers with a few through and through sutures.

During the operation the patient was given one pint of normal glucose saline and one pint of plasma. On returning to the wards the patient was kept on continuous oxygen inhalation, and coramine and strychnine 4 hourly.

Post-operative period.—For about six days following the operation the stomach had to be aspirated and washed with sodium bicarbonate solution, at least twice a day, as the patient would not tolerate continuous aspiration. The abdominal distension had also to be controlled with injections of prostigmine and the passage of a flatus tube.

The sutures were removed on the 12th day and the wound was found to have healed by primary intention. The patient was discharged on 3rd May, 18 days after the operation.

On 23rd May, about five weeks after the operation, the patient was examined. There was no apparent distension and no tenderness on palpation but the patient complained of vague abdominal pain and discomfort. This was relieved by a carminative mixture.

We are thankful to the Superintendent, Sir J. J. Group of Hospitals, for his kind permission to publish this case record.

TREATMENT OF HUMAN ANTHRAX WITH PENICILLIN

By S. AHMAD

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In view of the few publications so far on this subject, the following case report may be of interest.

A sepoy, aged 22, was admitted on 28th March, 1945, to this hospital with acute gangrenous inflammation

of the right ala of the nose and marked oedema of the adjoining portions of the face. Temperature was 103°, pulse 112, and the patient looked toxic and seriously ill. It appeared that local necrosis would need plastic repair later. A clinical diagnosis of anthrax was made, and confirmed by direct smear which showed morphological anthrax bacilli and staphylococci. The patient's shaving brushes were, however, found free of spores and the source of infection could not be traced.

In 1943 and 1944 I treated two cases of cutaneous anthrax in Iraq with sulphapyridine alone and with complete success.

In view of the severity of the case I decided to treat him with a combination of penicillin intramuscularly and sulphapyridine orally. In addition, penicillin solution, 500 units to 1 c.cm., was applied locally twice a day. The result was most satisfactory, both from point of view of control of toxæmia and of the local destruction of tissues. On discharge, the damage was found to be surprisingly limited and no plastic repair was necessary.

In view of the satisfactory results obtained with sulphapyridine, with penicillin, or with both, there would appear to be no indication now to employ the Sclavo serum, a treatment I found expensive, troublesome to the patient, and not so satisfactory as regards immediate response as well as the cosmetic result.

THREE CASES OF HÆMORRHAGIC SMALLPOX WITH RECOVERY

By K. C. SEN GUPTA, L.M.F. (Bengal)

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'HÆMORRHAGIC smallpox is always fatal' (Price, 1933); this sentence indicates the grave nature of this type of the disease. During the last year (1944) and the beginning of this year, a total of six cases of smallpox was admitted in the local F. R. E. Hospital. The first three cases were treated with sulphonamides and parenteral liver extract as described in a previous publication (Sen Gupta, 1944) and as in the other cases of smallpox, and all of them died. In the course of treatment of these three patients, it appeared that these patients could not be given adequate amounts of alkalies and fluids by the mouth on account of severe toxæmia, vomiting and unconsciousness. It was then decided to administer alkalies and solutions of glucose intravenously in such cases. Sodium bicarbonate 7½ per cent solution in 10 c.cm. doses intravenously was then added to the routine treatment with sulphonamides. The next three cases of hæmorrhagic smallpox were treated with this modified regime, i.e. intravenous sodium bicarbonate plus sulphonamides, and all of them made a more or less rapid recovery. The full clinical notes of these cases are presented below:

Case 1.—A Hindu male, aged 20 years, unvaccinated, was admitted on 30th March, 1944, on the third day of illness with hyperpyrexia and unconsciousness, with furious delirium at times. There was a dark purpuric rash over the forehead, arms and the thighs; the eyes were bloodshot with sub-conjunctival hæmorrhage. He was put on the following treatment—glucose 25 per cent solution 25 c.cm. intravenously twice a day, urea

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sulphazide 5 c.cm. intramuscularly, sulphapyridine 0.5 gm. two tablets, and neolivacon (liver extract) 2 c.cm. intramuscularly. Diet—'ghole', barley water, alkaline drink with lemon juice and sugar.

On the next day, only sulphapyridine 0.5 gm. and urea sulphazide 5 c.cm. intramuscularly, and from the third to the eighth day, only urea sulphazide tablets were given. The second dose of liver extract was given on the seventh day (3rd April, 1944).

During this period the temperature gradually came down, a vesiculo-papular rash developed, and there was little toxæmia.

On the ninth day of illness, the patient had a slightly higher temperature with hæmorrhages from the mucous membranes, epistaxis, blood with stools. Next day he was given sodium bicarbonate 7½ per cent solution 10 c.cm. intravenously twice daily, and sulphapyridine, liver extract and glucose injections. The fever came down to normal on the next day and the patient remained afebrile subsequently. The intravenous injection of sodium bicarbonate daily was continued till 10th April, 1944, along with sulphapyridine by mouth and glucose intravenously. He was later discharged as cured but with partial aphasia. The marks of decrustation were inconspicuous at the time of his discharge from the hospital.

Case 2.—A Hindu male, aged 14 years, unvaccinated, was admitted on 8th June, 1944, on the third day of illness in an unconscious state, with high fever (104°F.) and sub-conjunctival hæmorrhages, a dark red rash over the abdomen and the thighs. On the next day he had developed hæmorrhages around the eruptions. He was given an injection of 10 c.cm. of 7½ per cent sodium bicarbonate intravenously in the morning. In the evening the temperature had come down to 100°F. and the patient appeared to be partially conscious. The diet was the same as described in the previous case. On the next day, sodium bicarbonate injections were deliberately withheld and the patient put on sulphapyridine 1 gm. thrice daily. The patient had high fever 103°F., and the mental state grew worse, the temperature varying between 102°F. and 103°F., and more petechial eruptions appeared over the body. On the fourth day after admission, the intravenous injections of sodium bicarbonate 7½ per cent 10 c.cm. twice a day were recommenced, and only 1 gm. of sulphapyridine was given. (The diet and other treatment were the same all throughout.) By the evening the temperature had dropped to 100°F. and the patient was quite conscious. During the next four days, the patient was given sodium bicarbonate intravenously twice a day, and sulphapyridine 0.5 gm. thrice a day. His general condition rapidly improved. He was given 'half diet' (rice, dal, vegetables, milk and fish) from 16th June, 1944, and was discharged on 19th June, 1944. No liver extract was given.

Case 3.—A Hindu male, aged 30 years, unvaccinated, was admitted on 13th April, 1945, on the fourth day of illness, in a semi-conscious state, with temperature 100.8°F. The tongue was blackish in colour and very dry. He had minute ecchymotic patches over the forehead, thighs and abdomen. There were signs of catarrh over both lungs. In the evening the patient was found to be unconscious, with a temperature of 104°F., and there were sub-conjunctival hæmorrhages and signs of broncho-pneumonia. He was removed to the isolation wards next morning and put on injections of sodium bicarbonate 7½ per cent 10 c.cm. intravenously twice daily, and sulphapyridine 1 gm. thrice daily. The diet was the same as in the previous cases. Next morning the patient was afebrile and conscious. The pulmonary condition also showed slight improvement. On 16th April, 1945, the dosage of sulphapyridine was reduced to 0.5 gm. thrice a day; it was omitted from the next day. The injection of sodium bicarbonate was continued for a day more (up to the 18th). The patient remained afebrile from the 16th, the eruptions gradually grew inconspicuous and the lung signs disappeared. Except for general weakness, the patient was apparently quite well on the sixth day after admission. The diet was gradually increased

and he was discharged as cured. There were no marks of any rash on his body.

Conclusions.—The above three patients, seriously ill with hæmorrhagic smallpox, an invariably fatal condition according to well-recognized authorities, made a recovery under a regime of treatment that consisted essentially of intravenous administration of sodium bicarbonate and glucose, sulphonamides orally and parenterally where required, along with alkalies, vitamin C by the mouth. This fact leads the writer to consider that the regime of treatment adopted in these cases is worth further trials in different hospitals in a larger series of cases of hæmorrhagic smallpox in order to assess its value. It is likely that this treatment may also be of value in non-hæmorrhagic cases of smallpox. This point is also worthy of consideration by other workers in charge of larger infectious diseases hospitals in this country.

The writer is thankful to Dr. L. E. Crean, Additional Civil Surgeon, Mymensingh, for his kind permission to publish this paper.

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SEN GUPTA, K. C. (1944). *Calcutta Med. J.*, 41, 141.

TWO UNUSUAL CASES OF CEREBRAL MALARIA

By D. C. MAJUMDER, L.M.P. (Assam)
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Doom Dooma, Upper Assam

THIS year, while treating cases of malaria, I saw the following two cases of cerebral type :

(1) Infant, aged about 1 year, admitted on 26th April, 1945, at 6 a.m. in an unconscious state with persistent convulsions; pulse could not be counted; general appearance toxic; temperature 98.4°F.

On examination, there was stiffness of neck with backward retraction of the head; eyeballs rolled upwards, with contracted pupils, reacting to light; marked lockjaw with dripping of saliva; Kernig's sign positive; spleen enlarged 2 fingers; hæmoglobin value 45 per cent (Tallqvist). Convulsions were epileptiform in character and persisted for 30 hours. Peripheral blood showed abundant B.T. rings and schizonts.

(2) Infant, aged 1 year, admitted on 30th April, 1945, at 8 a.m. Temperature 98°F., and persistent convulsions. Spleen enlarged 2½ fingers; hæmoglobin value 45 per cent (Tallqvist); other symptoms like case (1). Peripheral blood showed abundant B.T. rings and schizonts. Convulsions persisted for 12 hours. Stool and urine examinations were negative in both cases.

Treatment.—After an enema, treatment of malaria with quinine was given parenterally. In both cases the temperature went up after the injections: in the first case up to 102°F. after 12 hours and in the second case 99°F. after 36 hours of admission. Rectal bromides, whiffs of chloroform and icebags were applied. Both the cases showed gradual improvement and recovered.



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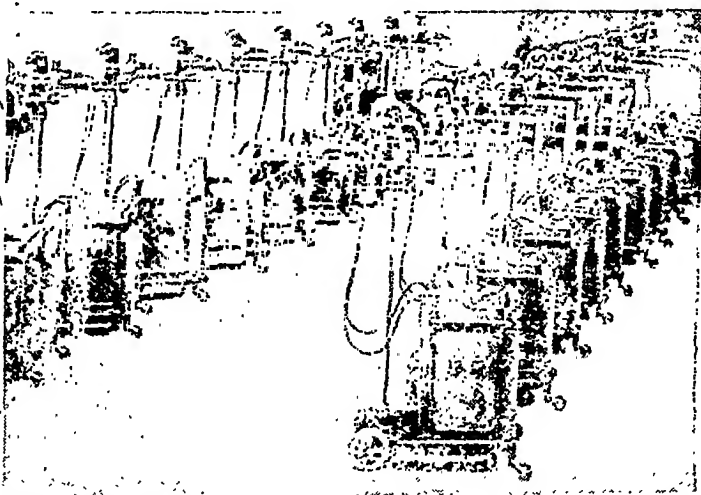
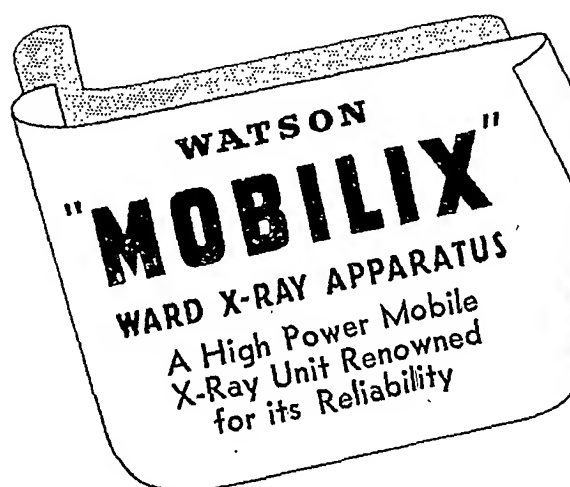
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Indian Medical Gazette

DECEMBER

BURNS AND SCALDS

BURNS have been very common in the war that has just ended, but as yet there is no general agreement about their treatment. Much progress has no doubt been made, but still there are many unsolved problems, of which the chief are shock, infection and severe protein depletion. In view of the urgent need of the war, the Medical Research Council initiated a research unit in the Glasgow Royal Infirmary which, by the way, receives more cases of burns than any other hospital in the British Isles and which has special wards for their treatment. Its report* which was issued early this year embodies observations made in 1942-43 on some 400 in-patients and nearly 2,000 out-patients, a brief summary of which is given below.

In severe or extensive burns, first-aid should not be attempted other than keeping the patient warm and giving morphine. What chiefly matters is to get him to hospital. In other cases, avoidance of infection by the hæmolytic streptococcus is the main consideration. For most burns which are accessible, first-aid should usually be limited to covering the injured part with a sterile cloth or, at least, a recently laundered clean towel. When superficial small burns are treated at home, or when, in the case of more severe burns, the plenary treatment cannot be carried out without considerable delay, they may be smeared with a cream containing 1 per cent cetavlon (a new synthetic detergent, cetyl trimethyl ammonium bromide) and 3 per cent sulphanilamide and then wrapped in sterile lint and bandage, or in a clean towel. Before applying the cream, no washing is to be done, nor should blisters be snipped. The cream should be removed in two days, because of a slight risk of dermatitis. The first-aid must be carried out with aseptic precautions—thorough washing of hands, wearing a mask or clean handkerchief over nose and mouth, applying the cream with a knife blade or spoon previously sterilized by boiling, etc. Blankets should on no account be allowed to come into direct contact with the burn as they are often heavily contaminated.

For the control of infection, the plenary treatment adopted at Glasgow relies largely on thorough cleaning, under aseptic precautions, of

the burnt area with 1 per cent cetavlon solution, ordinarily under morphine. Almost complete sterility is usually obtained, except in cases burnt more than 24 hours previously. After cleaning, a bacteriostatic dressing in the form of a mixed sulphanilamide cream is applied, its formula being sulphanilamide 3 gm., sulphathiazole 3 gm., glycerine 10 gm., castor oil 25 gm., lanette wax SX 10 gm. and water 49 gm. The burn, which must be widely covered and firmly bandaged, is left untouched for 7 to 10 days or even 12 days unless the affected part is such that some amount of contamination is unavoidable. There may be some fever during the first 2 or 3 days from reaction to the injury, but the dressing should not be changed unless the part is unduly painful and the patient's general condition suggests an acute infection. For burns already infected, penicillin or propamidine cream was found very efficacious. Thirty per cent of the patients admitted without hæmolytic streptococci acquired them during the first week, and in later stages coliform bacilli, proteus and *Ps. pyocyaneus* were often found. They were obviously due to cross infection in wards. The opportunities for such infection must be reduced, and 'we must work out a system of preventive measures, analogous to those of the operating theatre but appropriate to the different conditions obtaining in wards'.

Burns shock is responsible for the majority of deaths. The symptoms are seldom those seen in surgical shock. In children, drowsiness, restlessness, delirium, and, rarely, convulsions are the manifestations. In adults, such mental upset is rare; a phase of initial well-being is followed by coma. A rising temperature is common in the terminal stages and vomiting is frequent and severe. Hæmatemesis, even mild, is an ominous symptom.

In severe burns, loss of fluid occurs owing to increased capillary permeability; it is most rapid during the first 12 hours, and may continue until the third day. The plasma is lost from the circulation either as exudate or blister fluid—it may amount to several litres during the first three days—or into tissue spaces, and this also may be considerable. This leads to hæmoconcentration which is roughly proportional to the extent of the burn. Symptoms of shock develop in association with hæmoconcentration; they can be controlled by adequate transfusion as early as possible. Adults with burns of over 15 per cent of the body surface, and children with burns of over 5 to 10 per cent, generally require transfusion. The initial needs of any case should be decided by the severity, extent and duration of the burns, for if hæmoconcentration is allowed to develop over a period of several hours, there is little hope of overtaking the pathological processes by fluid replacement. The rate and magnitude of transfusion are best controlled by repeated estimations of red cells, hæmoglobin or hæmatocrit.

* Medical Research Council. Special Report Series No. 249. *Studies of Burns and Scalds*. (Reports of the Burns Unit, Royal Infirmary, Glasgow, 1942-43.) Published by His Majesty's Stationery Office, London. 1944. Pp. 210. Illustrated. Price, 4s.

levels. In the absence of blood readings, the blood pressure and pulse rate may be used as criteria, but are much less reliable. Reconstituted dried plasma in normal concentration has given much less reaction than liquid plasma. Much larger amounts than hitherto recommended are often necessary, owing to the partial escape of the fluid through the damaged capillaries, but transfusion given too rapidly or too great in amount may cause fatal pulmonary œdema, particularly in children. Good judgment is required to strike the happy mean between inadequate and too energetic fluid replacement. The amount required depends on several factors, *e.g.* the area, depth and site of the burn and age of the patient, and can be assessed only while the transfusion is being given, the rate being adjusted to produce and maintain a normal blood level. In most cases, local treatment during the shock period should consist of a first-aid dressing. Cetavlon solution is run over the whole surface, which is then covered with sheets of gauze, previously spread with the mixed sulphonamide cream already mentioned. Complete cleansing and dressing are postponed until the second or third day.

Another problem that awaits solution is how to deal with the severe *protein depletion* or other profound metabolic disturbances which so often kills patients afterwards and probably greatly delays healing in those who survive. In severe cases the plasma protein fails to regain normal levels or continues to fall despite large transfusions. These patients cannot take sufficient food to enable the protein intake to be kept up to replacement level. This can probably be overcome by giving protein digests intravenously or by intubation.

R. N. C.

REJECTED ARTICLES

THE editor of a medical journal has a difficult task to carry out. He wants to maintain a reasonably high standard in his journal; he wants at the same time to encourage the publication of any observation of interest and importance to the medical profession. He wants to encourage contributors; he wants to have friendly relations with the medical profession as a whole and with individual members of it. All these things are difficult to do simultaneously.

In some manuscripts received, the material is so badly presented that it is impossible to publish the material as it stands. In other manuscripts, while the presentation may be reasonably good, the data presented do not appear to justify the conclusions drawn. For these and for many other reasons, some articles submitted for publication have to be refused.

If the article is refused 'for lack of space', an author sometimes writes to enquire why

more space could be devoted to some other article of less value in his opinion. If the editor rejects an article for bad presentation or inadequacy of data and says so, he is apt to create ill feeling which may be expressed in personal abuse.

We try as far as possible to avoid these troubles. If a manuscript contains reasonably good data badly presented, we often accept it and try to improve the presentation; some articles appearing in our pages bear little resemblance to the manuscript which was originally received, the revision, however, being done if possible with the author's sanction. If, however, the data given in the article are unsatisfactory or inadequate for the conclusions drawn, there is little that we can do about it, and we have to reject the article because of our desire to maintain the reputation of the journal. If we do not, the journal, the editor and the author of the article lay themselves open to serious criticism.

Recently in a well-known medical journal appeared an article on the treatment of atypical pneumonia with human serum; only 10 cases were recorded, and the data appeared to us to be quite inadequate for the conclusions drawn. This article was recently abstracted in the *Bulletin of Hygiene* and the abstractor made the following comment:—

'The number of cases treated is small; the method of control is inadequate; and there is no exact comparison of two groups in regard to objective clinical criteria which might be used to assess rapidly of cure. The great variation between one case and another of this disease, the comparative "mildness" of a high proportion of the illnesses, and the tendency for many cases to show an early spontaneous remission of the fever suggest that any therapeutic measure demands the most careful control, preferably by the treatment of alternate cases. This report does not make out a good case for the method of treatment described.'

The same criticism can be made of many articles actually published, and unless an editor exercised his function in rejecting such articles the number of such published articles would greatly increase. The reputation of not only the journal and the editor, but also of the author suffers from such publications.

Recently we had an unusual experience. We had received, a year or two ago, a paper which was rather wildly speculative, and we refused it on the basis that the data were insufficient for the conclusions drawn, rather to the annoyance of the author. Within a few months other papers appeared which showed that the conclusions of the rejected article were completely erroneous. We recently received a letter from the previously disgruntled author expressing his gratitude to us for having, by refusing to publish his paper, prevented him from making a fool of himself in print.

Such experiences are few, but we hope that it will be realized that an editor acts not only in the interests of his journal, but of the author as well as the medical profession, when he

carries out the unpleasant task of refusing an article for publication.

J. L.

Special Article

THE ORGANIZATION AND WORK OF AN ANATOMY DEPARTMENT

By A. M. KHAN, M.S. (Anatomy), M.B., M.S. (Surgery)
Professor of Anatomy, King George's Medical College,
Lucknow

THE reorganization of this department in the light of past experience and present trend is urgently called for. The matter will be discussed under the following heads:—

- A. Teaching.
- B. Research.
- C. Post-graduate training.
- D. Administrative considerations.

A. Teaching

Teaching in anatomy at present comprises lectures, demonstrations and piecemeal dissection on cadavers over a course of two years. Students learn in terms of deformed organs and discoloured structures rather than in terms of the body as a whole. They cram topographical details indiscriminately in an attempt to become 'good doctors.' Such details are easily forgotten as soon as the examination is over. Hence most of them cut a sorry figure at the bedside in senior classes. Ignorance of living anatomy and application of its principles to the art of diagnosis and treatment accounts for the existing state of affairs. It is unfortunate that the very object of teaching anatomy for two long years is defeated by rigid adherence to the present methods of instruction.

It is shocking to realize that two years are spent on assimilating gross details on cadavers without correlating such knowledge with the study of living anatomy. There can be no doubt that its teaching aims at imparting instruction on the structure and function of the living body. If so, how can this object be achieved without reference to living beings? It should also be appreciated that many anatomical facts and principles cannot be verified or understood even in a normal individual, e.g. lymphatic drainage, muscle action, joint movement, nerve distribution. But selected clinical material of the nature of cancer-breast, fracture, ankylosis, neuritis, cranial tumours, etc., can impress more convincingly than mere didactic lectures the importance of these fundamentals on which diagnosis and treatment are based. Why should medical students therefore be made to learn gross details, like students of zoology, and then be asked to forget most of them and

retain only a few facts of clinical importance? Why should they be made anatomists first and then clinicians later. To economize time and energy of students and to increase efficiency, the historical line of demarcation between pre-clinical and clinical teaching must shift to a new plane.

Reorientation of the present methods and revision of the existing curriculum in anatomy is a world-wide cry. The cry is to curtail 'dead house instruction' and insist on teaching of living anatomy (clinical and radiological) as well as principles of embryology and growth. The curriculum must provide the basic requirements of the 'general practitioner', and teaching should aim at imparting a clinical touch to the study of anatomy from the beginning instead of the end of the second year of medical studies. This is the only way that the time wasted in cramming of the minutiae of gross anatomy can be utilized in building up the modest edifice of 'living anatomy'.

B. Research

I am convinced that certain branches of human anatomy offer field for research in this country. Such investigations are not possible unless provision is made to put workers in touch with ill-understood problems pertaining to human welfare. The following paragraphs will deal briefly with the scope of anatomical research which can be undertaken, if access to clinical material is permitted.

1. *Clinical anatomy*.—Diagnosis and treatment are based on certain conceptions of anatomical principles; a reorientation of such ideas in the light of clinical experience is essential from time to time in order to improve diagnostic and therapeutic measures.

To debar students of anatomy from participating in the pursuit of such knowledge amounts to waste of trained labour and so much loss to the advancement of medical science. Let it be presumed that clinicians can set problems to anatomists. Who can deny that no research is possible unless the problem is conceived in its true perspective by the worker himself? If the anatomist is segregated from human material other than cadavers, can he ever be expected to contribute to the cause of clinical or experimental anatomy; a service for which he is better suited than many? In view of these considerations, it will be most desirable if anatomists and clinicians enter into alliance to tackle problems in different

branches of surgery by free use of facilities of either department.

2. *Applied embryology*.—This branch of anatomy offers a wide field for research. Teachers engaged in such work should naturally feel more interested in problems of clinical importance. Students will also benefit more from demonstration on cases presenting congenital defects than from mere didactic lectures. Does it not become imperative that ample clinical material should be made available to promote teaching and research?

3. *Post-natal growth*.—Work in this field offers a wide scope for teaching and research. Six eminent anatomists in Great Britain remark, 'we believe that it is desirable that students should be given more instruction on the post-natal growth of the body and its relation to nutritional and hormonal factors' (Appleton *et al.*, 1942). Realizing the importance of this recommendation from the view-point of general practice, the earliest opportunity was availed of to institute a 'Growth Study Centre' as a sub-section in this department under a research scholar Dr. Inderjit Singh. Detailed observations have already been made on 300 children from local schools and will be repeated every six months. The difficulties encountered in contacting, investigation and treating defective children are great but not insurmountable. All that is required is hospital facilities where such children can be kept under observation and treated.

4. *Medical anthropometry*.—This subject has received little attention so far in this country. Data dealing with body types and their predilection to disease are valuable to experts in preventive as well as curative medicine. An appreciation of this fact is responsible for anthropometric observations being made on medical students and on inmates of the Central Jail, Lucknow. More clinical material and facilities for studying it are needed.

5. *Radiological anatomy*.—An intimate knowledge of the normal provides the necessary background for detecting minor abnormalities in skiagrams. Such knowledge will permit early radiological diagnosis when other methods have failed. I know of no record of systematic investigations on these lines on a representative group of healthy Indians. The sanction of an x-ray plant for this anatomical department shows that authorities realize the necessity of such work. It is obvious that hospital facilities will be required for the proper conduct of such research.

6. *Medico-legal research*.—There is an ample scope for research in this field, which for various reasons should be undertaken by an anatomy department. Data regarding age changes constitute the major problem. Clinical material from in-patients and out-patients will facilitate such study.

The science of comparative anatomy and physical anthropology offer fields where human

material is not indispensable, but there are others who are better qualified than the medical staff of the anatomy department to contribute to these branches. There are, however, special sections on these branches in the museum of this department.

C. Post-graduate training

The importance of this function of a teaching department need hardly be emphasized. Provision has to be made for the following categories:—

1. Medical men who wish to obtain post-graduate qualifications in surgery or other clinical subjects.

2. Medical men who wish to make anatomy a career.

3. Others who apply for refresher courses.

The necessity of hospital facilities for the students of the first category is obvious. Such provision will benefit them as well as the students of living anatomy who will attend the wards for necessary instruction. Refresher courses will have to be planned on similar lines. The need for training in pure anatomy has not so far been felt, but conditions may change in the future, and steps have to be taken to develop special sections under each teacher with this end in view. A move has already been made in this direction.

D. Administrative considerations

Among 12 teachers recruited on a permanent basis between 1911 and 1945, only one remained in the department, that too, for personal reasons. The rest left at the earliest opportunity with a view, in most cases, to taking up clinical appointments. Conditions of service must be made attractive enough to retain the services of highly qualified men for teaching and research in anatomy.

Conclusion

From the above it is obvious that the historical line of demarcation between pre-clinical and clinical studies must shift to a new plane. Teaching in anatomy should be so organized as to impart a clinical touch at the earliest opportunity. To effect this, it is essential that the department should be adapted to its primary function of equipping the under-graduate with the fundamentals and basic principles of living anatomy from the very beginning. This will enable him to steer comfortably through his clinical studies without being encumbered with unnecessary details of 'dead house' instruction. With this object in view the following suggestions are submitted:—

1. 500 hours in the first year and 250 hours in the second year should be spent on dissection and lecture-demonstrations on gross anatomy, embryology and post-natal growth, leaving the rest of the time for other subjects of the pre-clinical and transition periods.

2. Instruction in living anatomy should start in the second year on the lines suggested in this paper, and students should attend wards regularly for 1 to 2 hours daily.

3. In all medical colleges and schools, adequate provisions should be made for a clinical anatomy unit properly staffed for work in the hospital for teaching and research on clinical anatomy.

REFERENCE

APPLETON, A. B., *et al.* (1942). *Brit. Med. J.*, *i*, 196.

(The teaching of anatomy has been the subject of much study and discussion abroad, and it is good that the subject should be considered in this country. Some of the criticisms of anatomical teaching made in this paper may not apply to all departments of anatomy. Thirty years ago living models were used for some anatomy teaching in the editor's medical school, and this has since been much developed. Many of the criticisms are however still true of many departments of anatomy.—EDITOR, *I.M.G.*)

Medical News

THE INDIAN HONOURS LIST

1ST JANUARY, 1946

THE following are the names of medical men, and others associated with medical institutions, in the Indian Honours List of date 1st January, 1946. We offer them our congratulations.

K.C.I.E.

Major-General (Local Lieutenant-General) J. B. Hance, C.I.E., O.B.E., I.M.S., Director-General, Indian Medical Service.

Major-General H. J. M. Cursetjee, C.S.I., D.S.O., K.H.S., I.M.S. (Indian Army Medical Corps), lately Deputy Director of Medical Services, North-Western Army.

Colonel S. L. Bhatia, M.C., I.M.S., Inspector-General of Civil Hospitals, Assam, and lately Deputy Director-General, Indian Medical Service.

Knighthood

Lieutenant-Colonel N. S. Jatar, C.I.E., D.S.O., I.M.S. (retired), Inspector-General of Prisons, Central Provinces and Berar.

Lieutenant-Colonel S. S. Sokhey, I.M.S., Director, Haffkine Institute, Bombay.

F. Ware, Esq., C.I.E., Director of Animal Husbandry, United Provinces.

C.B.E.

Lieutenant-Colonel R. B. Billimoria, Honorary Medical Specialist, Indian Military Hospital, Bombay.

O.B.E.

Mrs. Robina Margaret Gertrude Brown, lately Regional Commissioner, Indian Red Cross Society, N.-E. India, Bengal.

Lieutenant-Colonel C. A. Bozman, I.M.S., Officiating Public Health Commissioner with the Government of India.

Major J. Singh, I.M.S., Deputy Director, Malaria Institute of India.

H. E. Rawlence, Esq., Residency Surgeon, Srinagar, Kashmir.

Colonel C. G. Terrell, lately Member of the Assam Legislative Assembly, Medical Officer, Indian Tea Association, Assam.

M.B.E.

Mrs. Wynne Butler, Chairman, Indian Red Cross Women's Council, Bombay.

Miss Louise Lyall, Matron, Cadets Hospital, Indian Military Academy, Dehra Dun.

Mrs. Dorothy Stanier, Lady District Superintendent, Auxiliary Nursing Service, St. John Ambulance Brigade Overseas (District No. 3), Bombay.

Captain A. R. P. Imam, I.A.M.C., I.M.S., Attached to No. 2 I.B.C.H. (I.T.), and lately Sub-Divisional Health Officer, Feni, Bengal.

Captain N. P. Billimoria, Honorary Ophthalmic Surgeon, Indian Military General Hospital, Bombay.

H. C. Edmunds, Esq., Medical Missionary, Hiranpur, Santal Parganas District, Bihar.

P. C. Guha, Esq., Civil Surgeon (retired), Assam.

A. K. Nulkar, Esq., Civil Medical Practitioner, Indian Military Hospital, Poona.

Rai Bahadur R. S. Srivastava, Civil Surgeon (retired), Dehra Dun, United Provinces.

R. L. Tuli, Esq., Deputy Director of Public Health (temporary), Central Provinces and Berar.

Major C. M. E. Warner, Port Health Officer, Calcutta.

Kaisar-i-Hind Gold Medal

Miss Madeline Shearburn, M.B.E., Doctor-in-Charge, Zenana Mission Hospital, Tank, North-West Frontier Province.

J. W. Bottoms, Esq., Medical Missionary, Baptist Mission Hospital, Chandraghona, Chittagong Hill Tracts, Bengal.

Kaisar-i-Hind Silver Medal

Mrs. Wenonah Ansorge, Chairman, Joint War Committee of the Indian Red Cross and St. John Ambulance Association, Bihar Branch.

Mrs. Avis Gladding, Chairman of the Ladies' Sub-Committee of the Countess of Dufferin Hospital, Calcutta.

Miss Wilhelmina Beatrice Greenwold, Assistant Doctor, Zenana Bible and Medical Mission, the Kinnaird Hospital, Lucknow, United Provinces.

Mrs. Christabel Phyllis Humphreys, Secretary, Red Cross Society, Coorg.

Mrs. Ailsa Margaret France Meyrick, Honorary Secretary, Red Cross, Motihari, and Honorary Secretary, Girls' School, Bihar.

Mrs. Mary Alexander Silver, Lady Doctor and Missionary Worker, Arkonam, North Arcot District, Madras.

Miss Bernard Valentine (Sister, Saint-Remi), Matron, Government Erskine Hospital, Madura, Madras.

R. Easy, Esq., I.M.D., Assistant Residency Surgeon, Bushire, Persian Gulf.

The Reverend A. G. MacLeod, Missionary, Honorary Superintendent, F. R. E. Hospital, Naogaon, Rajshahi, Bengal.

V. G. Mahajani, Esq., Doctor and Landlord, Satara, Bombay.

J. C. Paymaster, Esq., Chief Surgeon, Tata Memorial Hospital, Bombay.

T. Roy Chowdhury, Esq., General Secretary, Gocharan Ramkrishna Sevasram, 24-Parganas, Bengal.

Bar to the Kaisar-i-Hind Silver Medal

Mrs. Gladys Evelyn Waight, Honorary General Secretary, Diversional Therapy Services, Calcutta.

Kaisar-i-Hind Bronze Medal

Mrs. Sheila Christine Cunliffe, Voluntary Red Cross Worker, Bombay.

Mrs. Kathleen Forester, Red Cross Hospital, Supplies Section, Calcutta, Bengal.

Miss Bhagwan Devi Jessaram Kathuria, Doctor-in-Charge, Lady Willingdon Zenana Hospital, Jacobabad, Sind.

Mrs. Mavis Ker, Lady Divisional Superintendent, No. 1, Calcutta City Nursing Division, St. John Ambulance Brigade, Overseas, No. II, Bengal District.

The Reverend Mother Mary Odile, Ursuline Order of Nuns (R. C.), Nursing Sister, Ranchi Sadr Hospital, Bihar.

Mrs. Leslie Hamilton Shirlaw, Secretary, Provincial Red Cross Office, Lucknow, United Provinces.

Mrs. May Ronaldson Stephen, St. John Ambulance Brigade, Calcutta.

Mrs. Elizabeth Stribbling, Honorary Treasurer of the Rawalpindi Nursing Division, Punjab.

Mrs. Vinnala Surve, Honorary Secretary, Kolhapur Residency Red Cross Centre and Honorary Assistant Technical Recruiting Officer for the Women's Auxiliary Corps (India), in the Deccan States, Kolhapur.

Mrs. Edith Thick, Accountant, Punjab Red Cross War Depot, Punjab.

Mrs. Francon Williams, In-charge of Red Cross Work, Doonars, Bengal.

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Vaidyaratna

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K. B. L. Varma, Esq., Medical Practitioner, Meerut, United Provinces.

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Lala B. Nath, Agency Surgeon (Officiating), South Waziristan, North-West Frontier Province.

B. L. Juneja, Esq., Registrar, Indian Red Cross and St. John War Organization.

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Rao Sahib

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E. S. Reddi, Esq., District Health Officer, Madras.

T. V. Mudaliyar, Esq., Livestock Development Officer, Civil Veterinary Department, Madras.

C. H. A. Venkateswaran, Esq., Assistant District Medical Officer, Coimbatore, Madras.

P. Ramanujachari, Esq., Medical Practitioner, Cocanada, East Godavari District, Madras.

P. Srinivasan, Esq., Medical Practitioner, Madras.

C. H. S. Verma, Esq., Medical Officer-in-Charge, Civil Hospital, Mawana, Meerut District, United Provinces.

V. R. A. G. Krishnan, Esq., Veterinary Investigation Officer, Gauhati, Assam.

V. G. R. Mudaliar, Esq., Sub-Assistant Surgeon, Veloo Mudaliar Dispensary, Bangalore.

R. R. Rishi, Esq., In-charge, Electrical and X-Ray Department, Maharaja Tukojirao Hospital, Indore State, Central India.

K. Satyanarayan, Esq., Second Medical Officer, Bastar State.

O.B.I.

To the First Class with the title 'Sardar Bahadur'

Indian Army Medical Corps

Subedar-Major Ram Saran Mehra, *Bahadur*, O.B.I.

Subedar Attar Singh Chatwal, *Bahadur*, O.B.I.

Subedar-Major Mahtura Dass, *Bahadur*, O.B.I.

Subedar Sunder Singh, *Bahadur*, O.B.I.

Subedar-Major Kanshi Ram, *Bahadur*, O.B.I.

Subedar-Major Inder Singh, *Bahadur*, O.B.I.

Subedar Mohan Lal, *Bahadur*, O.B.I.

Subedar-Major V. N. Deuskar, *Bahadur*, O.B.I.

Subedar Richpal Singh (I), *Bahadur*, O.B.I.

Subedar-Major Inder Singh Rawat, *Bahadur*, O.B.I.

Subedar-Major Nand Kumar Tiwari, *Bahadur*, O.B.I.

Subedar-Major Faqir Chand Kapila, *Bahadur*, O.B.I.

Subedar-Major Mathura Prosad, Sati, *Bahadur*, O.B.I.

To the Second Class with the title of 'Bahadur'

Subedar-Major and Honorary Lieutenant Hira Singh.

Subedar Mirza Ali Ahmed.

Subedar-Major Niranjan Singh.

Subedar Nur Singh.

Subedar-Major Rodh Rai Bali.

Subedar-Major Hazura Singh.

CLINICAL MEETING AT THE SCHOOL OF TROPICAL MEDICINE, CALCUTTA

At the third clinical meeting of the Calcutta School of Tropical Medicine held on the 5th December, 1945, Major-General W. E. R. Dimond, R.M.S., outlined the medical administration of Bengal with particular reference to the special hospitals established during and after the famine, which are still being maintained as part of the provincial medical administration. These hospitals provide accommodation for altogether about 20,000 patients, and the accommodation is well utilized. They are small hospitals located in different parts of the province according to local needs and are grouped so that no patient has very far to travel to reach a hospital.

Dr. A. K. M. Abdul Wahed showed an atypical case of post-encephalitic Parkinsonism, the abnormal

features being the presence of a marked unilateral lordosis and also evidence of a pyramidal lesion in the internal capsule presumably of a thrombotic origin producing a left hemiplegia. The pyramidal and extra-pyramidal lesions appeared about the same time.

Dr. Wahed also showed a case of Cushing's syndrome in a married woman aged 20, the main complaints being obesity, abnormal growth of hair, palpitation, weakness and thirst. The areas of accumulation of fat were tender on pressure and showed striæ; there were tachycardia, hypertension, osteoporosis in the tibia and fibula; the sugar tolerance test showed a diabetic type of curve, but there was no hyperglycæmia or glycosuria. Polycythæmia was not present. The prognosis and treatment of such cases were discussed.

Dr. A. Das showed a case of pseudohypertrophic muscular dystrophy with Pink disease in a child aged six years. The disease started with disinclination to walk; later there was inability to rise and to walk normally, stiffness of the muscles of the arm and leg. In spite of this the child gained in weight. The child showed marked redness of the face and extremities with swelling but not pitting on pressure. The nervous system was normal; the calf and arm muscles and latissimus dorsi were hypertrophied; the glands of the neck, axilla, and groin were enlarged; the spleen and liver were palpable.

Dr. R. N. Chaudhuri showed a case of pulmonary amœbiasis with symptoms of fever, cough, lassitude, loss of weight and pain in the chest. There was a patch of dullness and diminished breath sounds with a mottled opacity shown by the skiagram. There was a marked leucocytosis. Sputum examination revealed nothing. Sulphathiazole produced no effect, but the patient responded rapidly and strikingly to emetine and the radiological opacity disappeared.

Dr. J. Lowe showed three cases of epidemic dropsy occurring in railway employees at Jhajha where an outbreak of epidemic dropsy recently occurred. The mustard oil used was adulterated with *Argemone mexicana* in considerable amount.

Dr. Lowe also made a brief statement regarding nine cases of typhus seen in the hospital during the period of a few weeks, with one death. Four showed OXK agglutination, three OX19, and one OX2; in the other (fatal) case, significant agglutination was not obtained.

Dr. M. N. Bose, Principal, Carmichael Medical College, showed an exhibit of old and rare medical books including some first editions.

Dr. L. M. Ghosh showed a patient with extensive dermatitis suggesting pellagra but no other manifestation of this disease.

Animated discussion took place on most of these cases.

CLINICAL RESEARCH ADVISORY COMMITTEE, INDIAN RESEARCH FUND ASSOCIATION

At the first meeting of the above Committee held on the 24th August, 1945, the Chairman, General Hance, pointed out that from the notes submitted by the members all seemed to be agreed that while there was ample material available for clinical research, and that so far little use had been made of this. He defined clinical research as the discriminating use of the five senses, an objective approach to each problem, and the development and use of the critical faculties. He also quoted the view of Professor John Ryle that clinical research and clinical practice and teaching should go hand in hand.

Dr. V. R. Khanolkar said that during the many years of his association with the I. R. F. A. he was struck with the haste and amateurishness with which proposals for clinical investigation were submitted to the I. R. F. A., the consequent inability of the Scientific Advisory Board to recommend such proposals, and the resulting erroneous belief of the clinicians that the I. R. F. A. were not interested in their problems. He hoped that the committee would be able to assist their younger associates by offering them helpful suggestions

and timely criticism, and suggested that the common diseases occurring in different parts of India should be investigated simultaneously at different centres.

Dr. Kutumbiah, Dr. Kini, Dr. Goyle, Major Jaswant Singh and Dr. Hardikar spoke about the difficulties of junior research workers and of clinical research in their provinces, the lack of inter-departmental and inter-college co-operation, lack of adequate hospital records, etc. Lieut.-Colonel Goadby pointed out that the Clinical Research Advisory Committee should decide with regard to each proposal whether the problem had been isolated, whether the man concerned was capable of dealing with the problem, and whether that problem was capable of solution with the facilities available to the worker at the particular time, and that problems should be selected on which there could be a concentration of energy and available resources. He thought that the committee should get into closer contact with similar and more experienced organizations abroad. Lieut.-Colonel Andreassen and Dr. M. N. De also spoke. Lieut.-Colonel C. A. Bozman described the position of the committee in relation to the I. R. F. A. and the administrative side of the problem, and drew attention to the idea that the committee should have both short-term and long-term proposals.

After discussion at which the members outlined subjects which they considered should be taken into consideration, it was decided that those subjects mentioned below should be discussed by members with their colleagues and should form the basis for specific proposals to be submitted to the committee at their meeting in November: peptic ulcer (Madras-Bengal); infections of the feet (Madras); rheumatic infections; problem of essential hypertension in India; cancer in India, its incidence, clinical varieties and relation to conditions peculiar to the country; nutrition of surgical cases with special reference to water and mineral balance in Indian patients; cirrhosis of liver in infants and adults in India; periostitis, and general nutrition; the nutrition conditions in anæmia of the poorer classes; relapses and reinfection problems of malaria in different areas of India; amœbiasis; the complications of arsenical treatment; poliomyelitis in its earlier stages. The list was not arranged either in order of importance or urgency; nor was it suggested that it exhibited the possibilities of fields of clinical investigation in India.

Several resolutions were passed recommending the institution and co-ordination of clinical research in India, the establishment of close contact between the committee and research organizations abroad, better methods for keeping records in medical institutions, methods of selection of proposals, and of inspection of the work being done.

FOOD ADULTERATION

REENIVASAN, in an article in the *Indian Medical Journal* (15th December, 1945) on 'Pure Food', gives some common examples of adulteration of food. Adulteration of milk is the commonest practice and includes addition of water, cane-sugar, skimmed milk-powder, or buffalo's milk to cow's milk, while cream is often removed by skimming. In some instances, boric powder is added as a preservative. Agar is frequently used in commercial preparation of curds to give a richer look. Animal carcass fat, hydrogenated oils, vegetable tallow and various substitutes are common adulterants of ghee. Hawkers, posing to come from remote villages, sell vegetable fats as pure ghee. Butter has been found to be mixed with flour and contain as much as 60 per cent of water. Other common frauds include the addition of the cheaper ground-nut oil to gingelly oil, of mineral oils to coconut oil and of chicory and Bengal gram to coffee. At one time tea was heavily adulterated with black gram husk. Large quantities of turmeric powder were found in the Punjab to consist only of powdered rice coloured with a harmful organic dye, while lead was detected in a number of samples of curry powder in Madras.

SIR UPENDRA NATH BRAHMACHARI

RAI BAHADUR SIR UPENDRA NATH BRAHMACHARI, Kt., M.A., M.D., Ph.D., died at his Calcutta residence on the 6th February, 1946. Thus Calcutta has lost one of the most distinguished of its medical men.

Upendra Nath Brahmachari was born in 1875, son of a doctor. He qualified M.B. (Calcutta) in 1898, M.D. (Calcutta) in 1902, and Ph.D. (Calcutta) in 1904. He entered the Bengal Medical Service in 1898, and taught pathology and materia medica at the Dacca Medical School. Later he was appointed lecturer in the Campbell Medical School, Calcutta, a post which he held for nearly twenty years, and it was here that his best known work was done, namely, preparation of urea stibamine and its use in kala-azar. Sir Upendra Nath retired from Government service in 1927. He continued to take an active interest in medical research work and in the chemical industry until his death nearly twenty years later.

While his work in other spheres of medicine was by no means negligible, it was his work on kala-azar which overshadowed all his other work. It is not easy for us nowadays to realize what kala-azar was thirty or forty years ago, a very widely prevalent and usually fatal disease. It is true that antimony in other forms have been used in kala-azar in other countries and also in Bengal, but there is no doubt whatever that the introduction of urea stibamine in the treatment of kala-azar was a very great step forward. It can be given with relatively little trouble, it is so much less toxic than the preparations previously used, and in the majority of cases it was possible to give an adequate dosage so as to eliminate the infection. It is impossible to calculate how many lives were saved in India, and in Bengal in particular, by the introduction of urea stibamine twenty-five years ago. During these twenty-five years many other preparations have been introduced in the treatment of kala-azar but in the ordinary cases urea stibamine still holds its own.

During the last twenty-five years honours, titles and distinctions have been bestowed in large number on Sir Upendra Nath, and his services were called for by many bodies, not only for the distinguished position which he held, but for what he contributed in the form of service. Dean of the Faculty of Medicine, Calcutta University, and of the Faculty of Science, President of the Indian Science Congress, President of the Royal Asiatic Society of Bengal, these and dozens of other positions he filled with distinction. A mere list of the distinctions bestowed on Sir Upendra Nath would fill a whole column of this journal.

Soon after qualifying, Sir Upendra Nath started writing on medical matters, his earliest paper being in 1898. His medical publications altogether covered a period of nearly fifty years. They included publications on malaria, biliary cirrhosis, hæmolytic, and many other subjects, but of course his best known publications were his treatises on kala-azar. The collection of his published papers have in recent years been published by the Calcutta University Press in two volumes appearing under the title 'Gleanings from my researches'. A perusal of these volumes indicates the wide nature of Sir Upendra Nath's interests. He was interested in everything in medicine, but particularly in tropical medicine, and made contributions to many subjects. One important contribution which he made was the recognition of the condition now known as post-kala-azar dermal leishmaniasis.

Sir Upendra Nath was perhaps the first Indian medical man to attain a wide international reputation for his contributions to scientific knowledge of medicine, the first of a large and growing band of Indian research workers. His passing would be mourned by many in India and throughout the world.

SALMONELLA INFECTION

MAJOR William Hayes and Captain Joseph F. Freeman, in an article on 'The incidence, type and bacteriology of Salmonella infection in the Army in

India' in the *Indian Journal of Medical Research*, October 1945, present a survey of these organisms studied from 1941 to the beginning of 1945. During this period, a total of 1,847 organisms of the *Salmonella* group were received in the Central Military Pathological Laboratory (formerly the Enteric Laboratory, Kasauli) for verification of diagnosis. Of these, 1,299 were identified as *Bact. typhosum*, leaving a balance of 548 organisms of other types. The number of isolations of *Bact. typhosum* rose from 1941 to 1942 but thereafter declined (the incidence of enteric per 1,000 of the Army in India has actually fallen throughout the period). During the period, *Bact. paratyphosum A* has next to *Bact. typhosum* been most prevalent, while the incidence of *Bact. paratyphoid B* was rare, but that of *Bact. paratyphosum C* and *Bact. enteritidis* shows a significant and progressive rise from 1943.

The great majority of *Bact. paratyphoid C* cases occurred sporadically in areas associated with the Burma campaign. It is believed that this infection is common among the Chinese, and it has been suggested that it may have been introduced into India by Chinese personnel. It is also possible that the movements of civilian population following the Japanese invasion of Burma may have played a part in its introduction. All the strains of *Bact. paratyphosum C* were found to be biochemically typical in that they have invariably fermented arabinose. The differentiation of this organism from diphasic *Bact. cholerae-suis* which is antigenically similar was made by the demonstration of the presence of Vi antigen. In this infection there appears to be a definite tendency towards localized pus formation, five out of 102 strains being isolated from pus.

The type of *Bact. enteritidis* infection now encountered in India is usually a septicæmia with little or no evidence of preceding intestinal involvement. From the published accounts and the information accompanying these strains the cases appear to fall into 3 main clinical types. In the first there is spiky intermittent fever occasionally with mild diarrhoea, persisting for 1 or 2 weeks. The pulse rate is usually proportional to the temperature; the white cell count is normal, and there is no rash or splenic enlargement. In the second variety there is a long continued pyrexia of septicæmic type which may persist up to two months with or without leucopenia and relative bradycardia, but there is no rash. After a variable period, localization of pus formation is apt to occur. Abscess formation in the subcutaneous tissues, periostitis, empyema, meningitis or cystitis may be found. The third variety displays the full clinical picture of enteric fever with continuous pyrexia, splenic enlargement, rose spots, leucopenia and relative bradycardia. There is a tendency here, too, to localization and pus formation. The mortality rate is by no means uncommon (5 to 10 per cent). Out of ill strains of *Bact. enteritidis* isolated, all but one were biochemically typical in that both rhamnose and arabinose were fermented. *Dublin* variants ferment rhamnose only. All strains, both *Gaertner* and *Dublin*, fermented dulcitol, but while *Dublin* strains invariably fermented this sugar during the first 24 to 48 hours of inoculation, fermentation by *Gaertner* strains did not occur until after the fifth day and frequently much later. With one strain, acid was not produced until day of incubation. This is considered a point of considerable differential value and one which, it is believed, has not been reported before. The most important advances in our knowledge of the *Salmonella* group are that all members of the group are capable of giving rise to clinical manifestations, viz *Salmonella* fever, *Salmonella* septicæmia or *Salmonella* gastro-enteritis, and that any of them with the exception of *Bact. typhosum* and probably *Bact. paratyphosum C*, may be found in and be spread by animals, and that host adaptation may profoundly affect the course of human disease.

In view of the findings presented in this paper, the advisability of including in the TAB vaccine, the elements necessary to cover *Bact. paratyphosum C* and *Bact. enteritidis*, is worthy of consideration.

Public Health Section

THE WASSERMANN POSITIVE RATE OF CASES FROM HOSPITALS AND VENEREAL CLINICS OF CALCUTTA IN 1939, 1943, 1944 AND 1945

By S. D. S. GREVAL
LIEUTENANT-COLONEL, I.M.S.
A. B. ROY CHOWDHURY, M.B.
and

B. C. DAS, M.Sc.

(From the Imperial Serologist's Laboratory, School of Tropical Medicine, Calcutta)

In a paper in this journal last year (Greval and Roy Chowdhury, 1944) the writers gave

comparative figures for (i) a normal pre-war period in 1939, (ii) a period during the war, before the commencement of the anti-venereal drive in Calcutta in 1943, and (iii) a period after the commencement of the anti-venereal drive in 1944. To these they now add figures for 1945, for a period when the drive had passed its peak of activity, observations on the figures and associated considerations.

Observations on the figures and associated considerations

Incidence of syphilis.—The figures for 1939, 1943 and 1944 have been discussed below.

Table showing the Wassermann positive rate of cases from hospitals and venereal clinics of Calcutta in 1939, 1943, 1944 and 1945

Periods	Number of cases tested	Positive reactions, all grades (+, ++ and +++)		Strongly positive reactions (+++ only)	
		Actuals	Percentage of the total	Actuals	Percentage of the total
In 1939 :					
I. 11-4-39 to 8-5-39, 15 working days ..	1,000	146	14.6	55	37.7
II. 9-5-39 to 3-6-39, 16 working days ..	1,000	204	20.4	57	27.9
In 1943, before the anti-venereal drive :					
III. 2-1-43 to 23-2-43, 34 working days ..	1,000	235	23.5	91	38.7
IV. 23-7-43 to 29-8-43, 25 working days ..	1,000	275	27.5	51	18.5
In 1944, after the anti-venereal drive :					
V. 22-2-44 to 13-3-44, 13 working days ..	1,000	337	33.7	121	35.9
VI. 14-3-44 to 30-3-44, 10 working days ..	1,000	351	35.1	104	29.6
In 1945, after the anti-venereal drive had passed its peak :					
VII. 6-3-45 to 16-3-45, 8 working days ..	1,000	229	22.9	47	20.5
VIII. 19-3-45 to 29-3-45, 8 working days ..	1,000	221	22.1	46	20.8
IX. 25-6-45 to 10-7-45, 7½ working days ..	1,000	242	24.2	87	35.9
X. 12-7-45 to 20-7-45, 7 working days ..	1,000	255	25.5	87	34.1
XI. 1-8-45 to 10-8-45, 9 working days ..	1,000	253	25.3	85	33.5

Postscript (19-12-45)

The following figures have now become available :

Hospitals	Period	Total number of cases		Ratio of new to old cases
		New	Old	
Medical College V. D. Clinic	V and VI	1,566	5,143	1 : 3.28
	VII and VIII	940	9,668	1 : 12.85
	IX	338	2,038	1 : 6.02
Campbell V. D. Clinic	V and VI	1 : 3.0
	VII and VIII	1 : 6.0
	IX	1 : 5.0
Lady Dufferin V. D. Clinic	V and VI	218	606	1 : 2.77
	VII and VIII	119	1,510	1 : 12.68
	IX	112	999	1 : 8.91

Two conclusions emerge : (1) the apparent vagaries of periods marked VII and VIII are due to more treated cases being tested in these periods than in others, (2) the new cases have decreased markedly and steadily. This fact is not in favour of the increased incidence of syphilis in Calcutta.

The figures for 1945 are of the same order and subject to the same interpretation. The relation between the strongly positive reactions (+++, indicative of secondary syphilis) and the total positive reactions (++ and +, indicative of syphilis of all stages) remains of the same order. The conclusion emerges that the incidence of syphilis in the civil population of Calcutta has not varied during the last six years. There are more cases attending clinics because there are more people in Calcutta. In 1939, 1,000 suspected cases could be collected from 1½ million of people in 15 or 16 days. In 1945, the same number is being collected from twice the population in half the time. The population has doubled itself since 1939 (Grevall and Roy Chowdhury, *loc cit.*).

As a matter of fact, when the publicity and free treatment of the anti-venereal drive are taken into consideration, one begins to wonder whether the incidence had not been actually reduced when the drive began. Such a probability is compatible with the malnutrition, discomfort and fatigue prevailing in the civil population, due to lack of food, accommodation and transport.

*Chunân qahat sâle shud andar Damishq
Keh mardum frâmosh Kardand ishq*

(Sa'di of Shiraz)

(One year there was such a famine in Damascus that people forgot how to love.)

Home comforts in India are often at the minimal level. A sub-minimal level could easily repeat what happened at Damascus. Doubleday's law of increased reproduction (and mating) in animals in a famine operates in the absence of discomfort and fatigue.

Sources of infection.—If, because of the increase in population, an increased number of cases are getting infected at the old rate per cent, it seems likely that the source of infection is constant. The infecting women have not increased so much as their clientele. This view is consistent with the housing and rationing difficulties that have existed in Calcutta during the period under reference.

If this view is correct, then the clinics have not benefited the infecting women. This is also consistent with the response that help evokes in prostitutes: while neither the rehabilitation nor treatment really succeeds as a rule, the former is given and received much more often.

Intensity of the reaction.—It has decreased. The +++ reaction of the writers is a reaction in which the last plus has been obtained with uncholesterinized antigen (Grevall and Roy Chowdhury, *loc cit.*). Typically it is a total inhibition of hæmolysis, although for the purposes of the report a mere trace of hæmolysis is ignored. ++T is accepted as +++. Since the anti-venereal drive began, more of the strongly positive reactions are ++T than

+++ . A decrease in the intensity of the reaction is due to decrease in the intensity of the disease, due to free treatment.

Total number of bloods tested for WR during a year.—From 1st October, 1944 to 30th September, 1945 (the date of preparation of this article), the total number of bloods tested in this laboratory, from Government and semi-Government hospitals in Calcutta and all venereal clinics in Calcutta, was 29,463. The figure for the financial year 1939-40 was 14,615.

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A NOTE ON THE SPREAD OF CHOLERA INFECTION THROUGH AERATED DRINKS

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CHOLERA infection is either eaten or drunk, and one of the problems confronting the health authorities is that of exercising rigid control on all articles of food or drink which are likely to serve as vehicles of infection. While the chances are that, during an outbreak of the disease, a large variety of articles of diet may become infected, yet, all such articles cannot be regarded as carriers of infection to the same extent. It is for this reason that health authorities, when armed with administrative powers, decide to prohibit the sale and consumption of certain foods and drinks. Our knowledge, however, of the precise part that each article of food can play in the spread of cholera is yet very limited, and it is more on the popular belief rather than on any scientifically proved facts, that certain articles are prohibited.

An analysis of certain foodstuffs in the Punjab with regard to their possible rôle in the propagation of cholera was made by Lal and Yacob (1926). They found considerable variation in articles of food in respect of the degree to which they promoted the growth of *V. cholerae*. For instance, whilst *moong dal*, boiled rice and milk were observed to be favourable for propagating cholera infection, such articles as curd, lemon and pickles were actually found to inhibit the growth of *V. cholerae*. It is, therefore, clear that the use of the latter class of foods could profitably be recommended during the cholera season especially

when that of certain other articles favourable for the growth of *V. cholerae* is prohibited.

No study, so far as we are aware, has yet been made to determine the precise rôle of aerated drinks. From personal enquiries we learn that their use is generally discouraged, and in some districts actually prohibited, when health officers are armed with special powers under the Epidemic Diseases Act of 1897. Aerated drinks are now extensively consumed all over the province and particularly in the towns. Their use is gradually extending to rural areas also. Moreover, the use of these is greater during that part of the year which is most favourable for the spread of cholera in this province, and on the occasion of fairs and festivals the indulgence in these drinks increases considerably. The study reported in this paper was, therefore, undertaken to investigate the part, if any, that these drinks play in the spread of cholera.

Technique

Known quantities of a 24-hour peptone culture were first placed in sterilized screw-capped bottles, and certain quantities of aerated waters were then introduced into such bottles. Caps were thereafter tightly screwed on. To prevent the escape of gas, the mouths of the bottles were dipped in melted paraffin. The aerated water was allowed to act on the *V. cholerae* for stated periods of time, after which the bottles were opened, and a small quantity, say, 2 to 3 c.c., was inoculated into alkaline peptone water with a pH value of 9.0. The peptone water was incubated for 24 hours at 37°C. Thereafter, 2 or 3 loopfuls from the peptone culture were streaked on plates of Aronson's medium which, after incubation for 24 hours at 37°C., were examined for shining red colonies of *V. cholerae*. Organisms from colonies of the likely colour were examined morphologically, and the identity of the cholera vibrios was confirmed by positive agglutination with 1 in 100 dilution of Inaba 'O' serum by the slide method. In all the experiments the test organism used was the Inaba strain of *V. cholerae* which, as well as the Inaba 'O' serum employed in the experiments, were obtained from the Central Research Institute, Kasauli.

At the factory, all the samples of aerated drinks were filled in at a pressure ranging from 120 to 150 lbs. The pH values of the soda water and of the original water used for the drinks were estimated at 6.8 and 7.8, respectively.

A series of experiments described in the following paragraphs was carried out to study the effect of varying the time of exposure of the vibrios to the action of aerated drinks.

Experiment 1

In each of 10 bottles, 0.1 c.c. of the 24-hour peptone culture of *V. cholerae* was exposed to

the action of 25 c.c. of plain soda water. The time of exposure was 24 hours.

As a control, another set of 10 bottles was inoculated with a similar quantity of culture in 25 c.c. of plain water which was being used in the factory for the manufacture of aerated drinks.

For the preparation of soda water, carbon dioxide was mixed with water at a pressure of 125 lbs. The pH values of soda water and plain water, as determined with Hellige's comparator, were 6.8 and 7.8, respectively.

It was found that whilst cholera vibrios could be recovered from all the 10 control bottles, in no case was the result positive for the soda water bottles. Thus, in a period of 24 hours, plain soda water appeared to have killed all the vibrios in 0.1 c.c. of culture.

Experiment 2

Instead of 0.1 c.c. of the peptone culture as in the previous experiment, 0.2 c.c. were inoculated in three bottles each containing 150 c.c. of aerated water. The time of exposure was only half an hour as compared with 24 hours in the first experiment. Three control bottles were also set up with 150 c.c. of plain water in each. These were inoculated with 0.2 c.c. of culture and were likewise exposed for half an hour. The gas was filled in at a pressure of 150 lbs. The pH values of soda and plain water were 6.8 and 7.8, respectively.

Cholera vibrios were recovered from all the six bottles, the fact indicating that half an hour was too short a time for the vibrios to die out under the action of soda water.

Experiment 3

The experiment 2 was repeated with 10 bottles in the soda water series, but the time of exposure was increased to one hour.

Out of the 10 soda water bottles, only three showed positive results, whilst from all the 6 bottles in the control group vibrios were recovered. Thus, a period of one hour also cannot be regarded as safe in practice.

Experiment 4

Bottles were set up as in experiments 2 or 3, but the time of exposure was increased to two hours. Only two bottles were taken as a control, but the number of those with soda water was 10 as in the previous two experiments.

From none of these 10 bottles could vibrios be recovered, whilst both the control bottles gave positive results. A period of at least two hours could, therefore, be reasonably expected to be sufficient as a lethal exposure.

Experiment 5

This experiment was designed to test the effect of aerated lemonade on the vibrios. Five bottles of aerated lemonade, each inoculated with 0.2 c.c. of the culture, were exposed for

2 hours. Five control bottles were set up as in the previous experiment.

The pH value of aerated drinks was 6.8 and of water in control bottles 7.8. The lemonade was aerated at a pressure of 135 lbs.

From none of the five bottles of aerated lemonade could vibrios be isolated whilst all the control bottles, as before, yielded positive results.

This experiment was repeated twice, and in all the three cases not a single sample showed a positive result.

It would thus appear that water contaminated with *V. cholerae* when frozen for 24 hours may be expected to become free from live cholera vibrios.

The results of the seven experiments are tabulated below :—

Experiment	Experimental medium	Control medium	Quantity of culture inoculated	Time of exposure	NUMBER OF BOTTLES					
					Experimental			Control		
					Positive	Negative	Total	Positive	Negative	Total
1	Soda water	Ordinary water	0.1 c.c.	24 hours	0	10	10	10	0	10
2	Soda water	Ordinary water	0.2 "	1 hour	3	0	3	3	0	3
3	Soda water	Ordinary water	0.2 "	1 "	3	7	10	6	0	6
4	Soda water	Ordinary water	0.2 "	2 hours	0	10	10	2	0	2
5	Aerated lemonade.	Ordinary water	0.2 "	2 "	0	5	5	5	0	5
6	Non-aerated lemonade.	Ordinary water	0.2 "	2 "	1	4	5	5	0	5
7	Soda with ice from infected water.	Water with ice prepared from infected water.	2-3 "	10 minutes	0	15	15	0	9	9

Experiment 6

In this experiment, the action of lemonade without aeration was studied on the vibrios. The experiment 5 was repeated with five bottles of non-aerated lemonade which also had a pH value of 6.8. Out of the five bottles, vibrios were recovered from one, thus indicating that non-aerated drinks were perhaps not so lethal as the aerated ones.

Experiment 7

Aerated drinks are ordinarily taken with ice. This experiment was designed to test whether ice could prove infective when taken with drinks in the customary manner.

Infected ice was first prepared by freezing, for 24 hours in a refrigerator, 1,000 c.c. of water to which 7 c.c. of a 24-hour peptone culture of *V. cholerae* had been previously added. Small cubes of this ice were prepared.

Plain soda water was poured into 5 beakers and into each, one block of infected ice was added. After about 10 minutes, when the ice had completely melted, 2 to 3 c.c. of the liquid were inoculated into alkaline peptone water. After an incubation of 24 hours, two loopfuls from each sample were streaked out on plates of Aronson's medium, and colonies were studied after 24 hours' incubation at 37°C.

Controls were set up by adding infected ice to three beakers containing plain water from the factory. In both the cases the results were negative.

Summary and conclusions

The generally unhygienic conditions under which aerated drinks are manufactured has given rise to the popular belief that these drinks are likely to propagate cholera. The health authorities are at present known to prohibit the consumption of these drinks at times of cholera outbreaks.

The experiments described in the paper, however, show conclusively that, given sufficient time, an aerated drink, even if infected with *V. cholerae* is rendered harmless by its own action on the vibrios. An exposure for a minimum period of two hours is necessary to kill all cholera vibrios. The pH value of aerated drinks is lower than that of plain water. It is, therefore, not possible, at this stage, to say whether the lethal effect is exercised more by the gas or by the acid reaction of drinks. It, however, seems clear that aerated drinks, as actually served, may be relatively more free from infection than water, and that their use could safely be recommended in times of cholera outbreaks.

It also seems likely that cholera infected water, when converted into ice and served in drinks, may also not prove harmful. The main conclusion to be drawn from the series of experiments reported in this paper is that it is unwise to prohibit or stop the consumption of aerated drinks during cholera outbreaks.

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A CASE OF CANINE *S. typhimurium* INFECTION WITH NOTES ON OTHER SALMONELLA INFECTIONS IN ANIMALS

The following is a summary:—

The subject of this note represents the second record of the isolation in India of an authentic salmonella species from the dog. The source was a cross bred female terrier aged about four years, which aborted after about a week's febrile illness. When first seen it had an acute septic metritis with signs of septicaemia and threatening collapse. The metritis cleared up rapidly under treatment but the constitutional symptoms persisted for about three weeks and were accompanied by a short but severe attack of enteritis, with blood in the faeces, lasting for about four days. Examination of the uterine pus revealed numerous coliform organisms, markedly phagocytosed. This organism was easily isolated by swabbing the uterine fundus and also from the faeces. Biochemical and serological experiments proving the identity of this organism with *S. typhimurium* are described.

A SURVEY OF LATENT DIPHTHERIA IN VIZAGAPATAM

The following is a summary:—

An account of an investigation into the carrier rate of *C. diphtheriae* in Vizagapatam has been given.

Swabs from the throat and nose of 707 children between 2 and 12 years of age were examined over a period of nearly 3 years.

C. diphtheriae was isolated from six of these children in none of whom were history or symptoms of diphtheria present. Four of the six strains were found to be virulent for guinea-pigs and two avirulent. The 'virulent carrier' rate for this locality was found to be 0.57 per cent and the 'avirulent carrier' rate 0.28 per cent.

AETIOLOGY AND TREATMENT OF *Ulcus tropicum*

The following is a summary:—

This paper gives a brief historical account of the disease with special reference to Bengal, describes the bacteriology of the causative organism, the cultivation of the fusiform bacillus, and the experimental production of sore, in detail, a brief discussion of the aetiology, and of the treatments adopted.

INVESTIGATIONS OF GROUND-WATER POLLUTION. PART II

Authors' summary:—

The mechanical, chemical and bacteriological properties of the soil medium, in which ground-water pollution studies were carried out in West Bengal, India, are described.

The soil was a sandy loam typical of alluvial deposits. The surface soil contained about 20 per cent clay, which gradually decreased with increasing depths. Below 16 feet, the soil was all sand. In the water-bearing region below 14 feet this sand was a homogeneous medium with about 40 per cent pore space and properties similar to a slow sand filter bed.

The soil was slightly acidic and well buffered by the presence of bicarbonates. It contained little organic matter and that present was of vegetable origin. Soluble minerals were not appreciable and were accounted for by carbonates, chlorides, and nitrates. Samples below 14 feet contained large amounts of free ammonia.

Bacteriological studies showed that gas-formers were present in large numbers in the soil but were definitely of non-faecal origin.

INVESTIGATIONS OF GROUND-WATER POLLUTION. PART III.

Authors' summary:—

An investigation of the nature and extent of pollution flowing from a bore-hole latrine into the ground-water was made at a site in West Bengal, India, during the period from September 1940 through April 1943. Preliminary studies were made of soil conditions, and the direction of ground-water flow and velocity were determined before the experimental field was completed and routine sampling of wells begun. The

results of the investigation may be summarized as follows:—

- A. Natural status of the ground water prior to seeding of the latrine:
 1. Bacteriological studies showed a concentration of lactose fermenters of from 3 to 8 per 1,000 c.c.m. of water, almost wholly of non-fæcal origin.
 2. Chemical analyses were made for pH, conductivity, chlorides, acidity, different forms of ammonia and B.O.D. Chemical constituents of the water varied significantly at different depths, zones and seasons.
 3. Water samples from wells above the latrine and from those not in the immediate direction of flow were examined at intervals throughout the period and the results used as an indication of the normal state of the ground water.
- B. Pollution flow following seeding of the latrine:
 1. The latrine was seeded with two gallons of night-soil on 330 days between November 1941 and April 1943. Septic action began in March 1942, and continued thereafter with undiminished vigour. The septic process only reached the ammonia stage. Only a fraction of the excreta added was disintegrated and at the close of the experiment there was a 2-foot column of sludge in the latrine.
 2. Routine observations were made of meteorological and ground-water conditions. Annual rainfall ranged from 40 to 80 inches, and the maximum slope of the water table was 1 in 200. Effect of seasonal changes on biological decomposition in the ground-water was not pronounced.
 3. Experiments on the true and false water-table near the latrine showed that the differences were not large enough to affect the flow of pollution.
 4. Six hundred gallons of water were pumped daily from wells situated 20 feet from the latrine in the direction of flow to simulate conditions of use of a village well.
 5. Bacteriological pollution was recovered in wells 10 feet from the latrine with large numbers of *B. coli* found in wells in the 5-foot zone over a period of two months. Numbers diminished later and the organism was virtually absent during the final period.
 6. Chemical pollution flowed with the stream to a distance of 15 feet. It was more intense in shallow than in medium or deep wells and was characterized by increase in conductivity, alkalinity, chlorides, acidity and ammonias. Nitrogenous products accounted for only a fraction of the pollution recovered.
 7. Organic matter indicated by the 5-day test for B.O.D. was recovered in the 5-foot zone. It was probably colloidal in nature and was filtered out beyond that point.
 8. Conductivity proved to be the most sensitive and hence the most satisfactory test for tracing chemical pollution.
 9. Chrysomias larvæ and their capsules were recovered from wells in the 5- and 10-foot zones where screens were damaged. They were found not only in wells in the direction of flow but all around the latrine.

STUDIES ON THE DESTRUCTION OF VITAMIN A IN SHARK-LIVER OIL. PART III

Author's summary:—
The rates of development of peroxides and of destruction of vitamin A at various temperatures are different. The vitamin is destroyed very rapidly after the termination of the induction period. More of vitamin A is destroyed for the same peroxide number at a higher temperature.

STUDIES ON THE DESTRUCTION OF VITAMIN A IN SHARK-LIVER OIL. PART IV

Author's summary:—
All the metals tested had a pro-oxidative effect on shark-liver oil, the order of the metals being: copper, mild steel, nickel, stainless steel, aluminium and tin, and zinc. Aluminium and tin had almost the same activity. At any peroxide number the percentage of vitamin A destroyed is the same with all metals tested

excepting copper. In the oil kept at 100°C. there was no accumulation of peroxides in the presence of copper.

THE GROWTH-PROMOTING VALUE OF EGGS. PART II

Authors' summary:—
A typical Bengali village diet gave very poor growth results, when fed to rats.
Eggs as the sole protein supplement to a Bengali diet gave good growth results but even better results were obtained with eggs plus calcium.
Supplements of soya beans, gram, green gram, red lentil, red gram and groundnut to the Bengali diet, all improved the growth rate but proved inferior to eggs.
The addition of calcium in the form of egg shell to the various vegetable protein supplemented diets had a beneficial effect on all the diets except that containing soya beans. With a calcium supplement, green gram and gram proved superior to soya beans. Green gram, gram and soya all proved superior to red gram, groundnut and red lentil supplements.
In the absence of a calcium supplement, soya beans as the sole protein supplement or in combination with egg proved superior to the other vegetable protein supplements.
Better results were obtained with all the vegetable protein supplements in combination with eggs than when fed alone.
From the purely economic aspect of human nutrition good results should be obtained with children from 6 to 9 years on a Bengali diet supplemented with one egg a day and the necessary amount of pulses to bring the protein level of the diets to 60 gm. per day.

BIOLOGICAL VALUE OF PROTEINS FROM MUSCLE MEAT OF COW, BUFFALO AND GOAT

Authors' summary:—
The average biological value of the protein of muscle meat from cow, buffalo and goat were estimated by the balance-sheet method at 10 and 15 per cent levels of protein intake. Ten per cent level of intake was found to be superior to that at 15 per cent. No significant difference could be found between the figures for buffalo-meat or goat-meat, whereas at 10 per cent level beef was found to be significantly superior to buffalo-meat or goat-meat.

THE FOOD VALUE OF A FURTHER BATCH OF EDIBLES

Authors' summary:—
Two kinds of grain foods, 7 kinds of flesh foods, 5 kinds of fruits, 9 kinds of mushrooms, 9 kinds of miscellaneous foods, 6 kinds of leafy vegetables and 2 kinds of milk products, in all 40 kinds of foods, have been analysed chemically as to their respective protein, fat, carbohydrate, moisture, ash, calcium and phosphorus content. The protein content of the 9 kinds of edible mushrooms varied between 2 to 7 per cent. Meat of mussel and immature shrimps gave high calcium figures. The list of foods included amongst others meat of field rat and bull frog and white ants which were listed as 'food consumed' during dietary survey operations in certain sections of population in Bihar.

STUDIES ON CALCIUM AND PHOSPHORUS METABOLISM. PART I

Authors' summary:—
The investigations described in this paper relate to diets in Kangra valley, Punjab, where abnormalities of calcium and phosphorus metabolism occur to a very marked degree resulting in a high incidence of rickets and osteomalacia. Some typical foods of Kangra valley were analysed for calcium, phosphorus and phytin contents and on the basis of those analyses the average diets of 14 different groups of the population of the valley were studied with regard to their calcium and phosphorus contents. The calcium content was low and phosphorus exceedingly high showing ratios of calcium: phosphorus between 0.08 and 0.22 for the various diets. This ratio is considered to be definitely low for proper calcification. For comparison seven

diets of population group from Central Punjab are also shown.

The rôle of phytic acid in the nutrition of the population of this area has also been investigated. From the phytic acid content of the foods grown in the area the available calcium and phosphorus of the diet, and the ratio of available calcium : available phosphorus have been calculated. This ratio is about 10 per cent lower than the ratio based on total calcium and total phosphorus. The presence of phytic acid therefore significantly aggravates the imbalance of minerals in the diets of these population groups.

A typical diet of Kangra valley was fed to young animals to study its effect upon (a) general growth and (b) development of bones. The growth on this diet was exceedingly poor, there being slight improvement when the diet was supplemented with calcium. The rate of growth even on the improved diet was only 25 to 35 per cent of the normal showing that there were other limiting factors involved. The skeletons of these rats were examined for their ash, calcium and phosphorus contents. The degree of calcification was poor in the case of animals fed on typical diet of Kangra valley, while the percentage of calcium and phosphorus in the bone ash together with the degree of calcification considerably improved for the animals whose diet was supplemented with extra calcium.

In another group of 18 rats on a typical diet of Kangra valley calcium balance was studied. All the animals were found to be on a negative calcium balance. On adding calcium to the diet so as to bring the ratio of calcium : phosphorus as 1 : 1, retention of calcium began to take place.

From these studies it is concluded that one of the chief abnormalities in the diets of the population of this area is the lack of balance of the minerals calcium and phosphorus.

STUDIES ON CALCIUM AND PHOSPHORUS METABOLISM. PART II

The following is a summary :—

The object of the present investigation was to study the blood conditions of the people in respect of calcium, phosphorus and phosphatase contents and to relate them to earlier findings. Blood examinations of the calcium, phosphorus and phosphatase contents were made on the patients attending the Civil Dispensary and Zenana Mission Hospital, Palampur. It was from these patients that normals as well as cases of rickets and osteomalacia were selected. The cases grouped as normals were those who had no ostensible signs of any pathological condition, and attended the hospital for only petty ailments. The selection of the rickets and osteomalacia cases was made on a clinical basis, and the degree of severity was assessed exclusively on the clinical symptoms and is based on the opinion of the medical officer in charge of the dispensary. The results are tabulated and statistically analysed. The results are discussed in relation to earlier findings and the findings of others.

STUDIES ON CALCIUM AND PHOSPHORUS METABOLISM. PART III

Authors' summary :—

Bone-ash determination and degree of calcification have been studied in guinea-pigs which were fed on carbon tetrachloride to produce liver damage. It has been observed that the degree of calcification is lower than normal controls, and that this difference is statistically significant.

The addition of oats to the normal stock diet had an additive effect upon the decalcifying action which is the result of liver damage.

The importance of phosphatase and its possible rôle in bringing about skeletal changes is discussed.

DENTAL AND OSSEOUS CHANGES IN SPONTANEOUS FLUOROSIS IN RATS

Authors' summary :—

A condition in rats, characterized by protrusion and mottling of incisor teeth, has been diagnosed from

histological examination of teeth and bones as fluorine intoxication.

The condition had occurred spontaneously in a colony of rats maintained on a diet from which the animals were presumably ingesting a toxic dose of fluorine. The fluorine concentration in the bones of some of the rats was much higher than that of animals kept on a low fluorine ration.

Histological changes in the bones and teeth of these spontaneous cases correspond closely to those of experimentally induced cases.

ASSAY OF ANTHRACENE PURGATIVES BY THE ESTIMATION OF THE CONTENT OF HYDROXYMETHYLANTHRAQUINONES. PART I

Author's summary :—

The hydroxymethylanthraquinone content of rhubarb obtained from various sources [European, Chinese, Sikkim (4 samples)] has been estimated.

The hydroxymethylanthraquinone content of rhubarb is a correct indication of the purgative potency. The purgative effect of these different rhubarb samples have been tested on cats, and it has been found that the effect is related to the hydroxymethylanthraquinone content. Samples of rhubarb containing about 2 per cent of hydroxymethylanthraquinone, even though they contain alcoholic extractive far below the minimum B.P. standard, are pharmacologically as effective as any B.P. standard rhubarb.

A modification of the present pharmacopoeial standard of purity of rhubarb is suggested.

ON THE PREPARATION OF LIQUOR ADRENALINÆ HYDROCHLORIDI

Authors' summary :—

Adrenaline solution as described in the British Pharmacopœia (1932) does not remain stable when incorporated with sodium bisulphite.

Sodium bisulphite lowers the physiological activity of the adrenaline solution. It should not be incorporated in any adrenaline preparation.

Mercuric formate of an organic acid salt of adrenaline does not ensure the stability of the solution.

Inula royleana DC : ITS CHEMISTRY AND PHARMACOLOGICAL ACTION

Authors' summary and conclusions :—

Inula royleana DC contains about 3 per cent of the alkaloid royleane having the empirical formula $C_{27}H_{45}O_4N$.

The alkaloid is not toxic to the free-living ciliates and has no bactericidal action.

The alkaloid produces fall in blood pressure and stimulates the tone and rhythmic movements of intestines on intravenous administration to the urethanized animals.

GLYCOLYSIS IN DIABETIC BLOOD AND ITS SIGNIFICANCE

Authors' summary and conclusions :—

The rate of glycolysis in diabetic patients has been found to vary according to the severity of the condition.

In severe cases of diabetes there is practically no glycolysis, even if the blood samples are left at room temperature for 24 hours.

In moderately severe cases of diabetes glycolysis proceeds at a very slow rate.

The rate of glycolysis in the blood of mild cases of diabetes does not differ materially from that observed in normal persons.

The glycolytic power of the blood of diabetic subjects who respond satisfactorily to specific treatment improves *pari passu* with improvement in the clinical condition of the patient, and in some cases, approaches that observed in normal subjects.

The height of the blood sugar level has been found to bear no relationship to the rate of glycolysis.

ON THE ASSAY OF UREA STIBAMINE

Authors' summary and conclusions :—

A selected batch of commercial urea stibamine has been adopted as a temporary standard for the assay of

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unknown preparations of urea stibamine. The chemical composition of the selected batch has been determined and a dose-response curve has been worked out in white mice.

The LD₅₀ figure for the selected batch of urea stibamine was found to be 215 mg./kg. for white mice of 18 g. to 20 g. weight. It is suggested that in the assay of unknown samples of urea stibamine a maximum variation of ± 30 per cent on this figure should be permitted. No significant difference in susceptibility was observed in male and female mice within the limit of weight stated above.

Solutions of urea stibamine are much more stable than solutions of organic arsenic compounds and it is not considered necessary in assaying urea stibamine to observe the elaborate precautions in the preparation and use of solutions which must be followed in the case of organic arsenicals.

The relationship between the total antimony content of urea stibamine and its toxicity is not yet known. As the chemical composition of urea stibamine is variable and as it is not yet definitely known which fraction or fractions are therapeutically active, the assay of unknown preparations of this drug should, for the present, be carried out by biological methods.

CHEMISTRY AND PHARMACOLOGY OF SOME COMMON INDIGENOUS REMEDIES

The following is a summary:—

This paper embodies the results of the studies carried out regarding the chemical composition and pharmacological action of *Aconitum heterophyllum* Wall, *Xanthium strumarium* Linn, and *Lippia nodiflora* Rich. These plants are widely used in indigenous medicine. Although they are reputed to possess certain medicinal properties and are quite commonly employed for such purposes, the observations show that, apart from the action of some known chemical substances which happen to be a part of the constituents of such plants, there is in the case of some an insufficient quantity of the active principles to produce any marked physiological action, and in case of others, the principle itself is inert and inactive.

HÆMATOLOGICAL STUDIES IN *Silenus (macacus) rhesus*. PART II

Authors' summary and conclusions:—Detailed hæmatological investigations by modern methods have been made in *S. rhesus* before and after infection with *P. knowlesi*. Observations were made throughout the course of an acute, fatal infection in one monkey. Subacute and chronic infections were induced by regulated quinine therapy and observations were made at regular intervals throughout these infections. Subacute infections were studied in 3 monkeys and chronic infections in 7 monkeys. The findings in infected monkeys have been compared and contrasted with those in uninfected monkeys. In all cases full blood counts were made including determination of MCV, MCH and MCHC. The results have been recorded in graphic form and discussed. On the basis of the observations made, the following conclusions have been reached:

The course of malarial anæmia in monkeys depends on the course of malarial infection but even among animals exhibiting the same type of infection, hæmatological reactions vary considerably.

The type of anæmia in monkey malaria is characteristically normocytic and orthochromic with a tendency towards macrocytosis at the lower levels of anæmia. The cause of this tendency has been discussed. Except in the terminal stage of an acute infection, van den Bergh (indirect) reaction is generally negative in monkey malaria.

In monkey malaria reticulocytosis of varying degree is observed. This is related more to the degree of anæmia present than to the administration of quinine injection.

The animals suffering from chronic malarial anæmia, death generally results from complications other than anæmia.

SPECTRA OF HÆMOCHROMOGEN AND CYANHÆMOCHROMOGEN

The following is a summary:—

There is a discrepancy in the illustrations or descriptions of the spectrum of hæmochromogen; according to some workers the right-hand band (on the observer's right), in the green, is narrower than the left-hand band (on the observer's left), in the yellow, while according to others the right-hand band is broader than the left-hand band. According to the present writers' evidence of the same discrepancy also exists with respect to the bands of cyanhæmochromogen. The right-hand band is stated and/or shown to be narrower than the left-hand band but the writers have produced photographs and described the process employed in taking the photographs to show that the right-hand band is broader than the left-hand band. Another discrepancy concerns the semblances of the spectrum of cyanhæmochromogen shown by cochineal, alkanet root and madder. These dyes are known to have spectra which superficially resemble those of hæmoglobulin derivatives. They are however stated not to have any such spectrum when treated as a blood stain is treated for obtaining the spectrum of cyanhæmochromogen. The writers find that cochineal when so treated produces a spectrum which can be mistaken for that of cyanhæmochromogen.

FILARIAL INFECTION IN DHAMDA (DRUG DISTRICT, C. P.) DUE TO *Wuchereria malayi*

Author's summary:—Dhamda in Drug District (C. P.), a moderately big village, has endemic filariasis, the infection being due to *W. malayi*. The micro-filaria rate is 13.3 per cent and the filarial disease rate is 2.2 per cent. Elephantiasis of the genitals, hydrocele and chyluria are entirely absent. The mosquito survey showed a prevalence of *Mansonioides* species. *Mansonioides annulifera* is the commonest mosquito in Dhamda and appears to be the chief transmitter of filarial infection. The breeding places are the large tanks covered with *pistia*.

A Case of DDT-Poisoning in Man

By V. B. WIGGLESWORTH

(Abstracted from the *British Medical Journal*, 14th April, 1945, p. 517. As abstracted in the *Bulletin of Hygiene*, Vol. XX, July 1945, p. 411)

This appears to be the first record of poisoning in man by the insecticidal powder, DDT; the symptoms closely resembled those observed in animals.

A laboratory worker, aged about 30, made experiments in which about 25 gm. of DDT, dissolved in acetone, was added to an inert dust and kneaded with his bare hands for some minutes, the mixture covering his hands almost to the wrist. On removal of his hands from the mixture, the acetone evaporated, leaving a dry deposit on the skin and this was removed by swabbing with acetone. There had also been a previous exposure of his skin in an experiment in which he allowed a small quantity of an acetone solution of DDT to evaporate on the back of his hand, the residual deposit being swabbed off with acetone.

From one to ten days later a feeling of heaviness and aching developed in all the limbs, with weakness in the legs. There was also what the subject described as spasms of extreme nervous tension. He took a holiday and improved, but on returning to work he became worse and three weeks later was confined to bed with constant aching in the limbs, sleeplessness, a feeling of extreme nervous tension and acute anxiety. Six days later, involuntary muscular tremors occurred over the whole body and these recurred at least twice. He got up after 10 to 14 days though his limbs still ached severely. He was absent from work for 10 weeks altogether but even at the end of a year he had not

quite recovered. Some of his anxiety was probably due to uncertainty as to the nature of the illness as no one suspected DDT poisoning, and he improved considerably when the diagnosis was made.

It is generally agreed that DDT causes no harm if used with discretion; the exposure in this case was far greater than would be likely to occur in practice.

Toxic Psychoses Following Atabrine

By H. S. GASKILL

and

T. FITZ-HUGH

(Abstracted from the *Bulletin of the U.S. Army Medical Department*, March 1945, No. 86, p. 63. As abstracted in *Tropical Diseases Bulletin*, Vol. XLII, August 1945, p. 629)

DURING seven months 35 individuals out of 7,604 cases of malaria admitted into an Army hospital in a highly endemic area where they were treated with mepacrine, developed toxic psychoses, 0.4 per cent. During the same period 197 acute psychoses, not related either to malaria or mepacrine, were treated in the hospital; this represents 3 per cent of the total admissions to hospital excluding admissions for malaria.

The patients were of two groups: group A, American soldiers, whites and negroes in about equal proportions; group B, soldiers of an allied nation. Most of group A had malaria for the first time; most of group B had had one or more attacks of malaria in the past. Of the 35 patients with post-mepacrine psychoses three were white and three negro Americans, and 29 allied soldiers.

The treatment was in accordance with the S.G.O. Circular Letter No. 135, 1942, the total amount of mepacrine administered being 2.1 gm. The time of onset of the psychosis varied, the most rapid being on the third day of treatment, after 0.9 gm. of mepacrine had been taken. The latest date of onset was twelve days after the completion of treatment. The most common date was six days after the completion of treatment. The onset of the psychosis was often insidious.

In some cases there was a sudden increase in motor and psychomotor activity with auditory and visual hallucinations and delusions. Occasionally there was disorientation. The effect was usually one of euphoria and expansiveness. In cases with insidious onset there was gradual clouding of the sensorium, disorientation and 'loss of recent memory'; and diminished activity in the intellectual and motor spheres. The patients were withdrawn and seclusive, the effect being one of bewilderment and fearfulness.

Infection with *P. falciparum* was twice as frequent as infection with *P. vivax* and this proportion held good for the patients who developed toxic psychoses.

Thirty-three of the 35 patients recovered, one in eight days, one in 85 days, the average duration of psychosis being 23 days. In the two patients who failed to recover it seems that a schizophrenic reaction had been precipitated. Complications occurred in three patients who recovered:—dislocation of the shoulder, cystitis from repeated catheterization, and spontaneous rupture of the spleen.

It is of great interest to note that 16 of these patients who had recovered from their toxic psychoses were retreated with mepacrine, 15 without any manifestation or untoward symptoms, the other becoming only mildly excited for 24 hours on the last day of treatment. The hypothesis of temporary desensitization to mepacrine as a result of an acute attack is compatible with the observations, but this is entirely speculative. Vitamin deficiency as a contributory cause of the psychoses is a possibility. There was no evidence that the patients who developed post-malaria-mepacrine psychoses were psychiatrically unstable (except, of course, as a result of taking mepacrine).

Psychosis Due to Mepacrine

(From the *British Medical Journal*, ii, 4th August, 1945, p. 162)

It is now common knowledge that the success of the Allied Forces in the Pacific in withstanding and then routing the Japanese invaders was greatly endangered in the earlier stages of the war by malaria, and that this danger has now been overcome mainly by the prophylactic use of mepacrine (atabrin). Mepacrine was first synthesized by the Germans in 1932, and its availability in 1942 (when the supply of quinine was cut off by the loss of Java) was an important factor in defeating Germany's ally. All powerful drugs have their disadvantages, and mepacrine is no exception: attention has been recently drawn again to the cerebral disturbances which occasionally follow its use. These disturbances have been noted at intervals ever since mepacrine was first used, but they are not common. Thus Kingsbury observed 12 cases of psychosis among thousands of Malaysians who had been treated; and Hoops had only one case of mental excitement among 1,207 cases of malaria treated. On the other hand, during the Ceylon malaria epidemic of 1935 Briercliffe recorded that 15 cases of delirium developed among some hundred persons who took the drug by mouth. Bispham in 1941 analysed the toxic effects seen when 49,000 cases of malaria had been treated with mepacrine; he noted that cephalalgia, mental depression, delirium, psychoses, and convulsions may occur; but the rate of incidence was very low. Field estimated the occurrence of mepacrine psychosis as less than 0.1 per cent of cases treated; the symptoms began just before or just after the end of treatment; the patients showed signs of excitement, confusion, or even mania, and the symptoms gradually subsided, after having lasted for approximately one week. Cerebral disturbances have occasionally occurred in the Australian forces, but they have been rare and have usually appeared in men who had taken excessive amounts of mepacrine during self-medication.

As regards diagnosis, the chief point is to exclude cerebral malaria, which should be suspected in all cases of peculiar mental reaction in the tropics until disproved. In psychosis due to mepacrine it should be noted that the patients have recently received anti-malarial treatment, that the slight initial fever which may be present in a few cases subsides in 12 to 24 hours, that the symptoms are all psychiatric, that the behaviour pattern remains constant, and that there is no objective neurological disturbance. The explanation of these cases is not clear. It is known that very large doses of mepacrine cause mental disturbances even in normal persons; but in the patients just described the dose was not abnormally high. Probably a combination of mepacrine, malaria, personal idiosyncrasy, and the hardships of warfare may be involved. Whatever the cause, it should be remembered that these toxic effects are rare and relatively unimportant compared with the damage which can be caused by malaria. It is interesting and useful to know that they can take place, but their possibility should never deter the confident use of this valuable prophylactic and therapeutic anti-malarial compound.

Estimation of Serum Proteins

By H. HOCH

and

J. MARRACK

(Abstracted from: the *British Medical Journal*, ii, 4th August, 1945, p. 151)

THE copper sulphate method for measuring specific gravity of serum gives satisfactory and consistent estimates of the protein concentration.

The apparent specific gravities found by this method are less than the true specific gravity.

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The equation recommended for calculating the protein concentration from the apparent specific gravity is $P = 364 (S - 1.006)$. For satisfactory and consistent measurements of serum protein by the Kjeldahl method, selenium dioxide should be used as a catalyst and digestion should be continued for at least one hour, and preferably for $3\frac{1}{2}$ hours.

Results of Penicillin Therapy

By R. F. FARQUHARSON
P. GREEY

and

S. R. TOWNSEND

(Abstracted from the *Canadian Medical Association Journal*, Vol. LIII, July 1945, p. 1)

MISCELLANEOUS INFECTIONS

Anthrax.—Two patients with anthrax were treated with systemic penicillin therapy (1,420,000 units); complete recovery.

Erysipelas.—Two cases were treated with systemic therapy. Spread of the infection was arrested and rapid recovery ensued.

Parotitis.—A case of prolonged acute *Strep. haemolyticus* parotitis unimproved by other measures, responded to systemic penicillin therapy by immediate improvement and apparent recovery. Two months later, however, there was a relapse.

FUSO-SPIROCHAETAL INFECTIONS

Excellent results from systemic therapy in fuso-spirochaetal infections were obtained. One patient with severe gingivitis had received local treatment of various types without improvement during twelve weeks in hospital. He was given 100,000 units of penicillin intramuscularly in six divided doses at three-hour intervals. There was immediate dramatic improvement. The smear was negative for fuso-spirochaetal organisms the next day. Similar good results from a total dosage of 100,000 to 300,000 units were obtained in patients suffering from ulcerative fuso-spirochaetal pharyngitis.

The use of penicillin pastilles has now become the method of choice in treatment of Vincent's infections. A penicillin agar pastille will maintain an adequate concentration of penicillin in the saliva for a period of at least four hours. Numerous cases have been treated with excellent results.

CARBUNCLES AND FURUNCULOSIS

Systemic therapy has been used in a number of cases of carbuncles and severe furunculosis. Good results were obtained when penicillin was used before the development of a large necrotic core. Such administration, although of great value in hastening the recovery from active lesions, did not prevent the subsequent occurrence of boils.

Clostridial infection.—Only one case with *Cl. welchii* infection was treated. The muscles of the left arm were involved. Recovery followed twenty-one days of treatment during which 120,000 to 240,000 units of penicillin were given daily. Radical surgery was combined with local penicillin therapy. In addition 50,000 units of anti-gas gangrene serum was given daily for five days.

Actinomycosis.—Results of penicillin therapy in five cases of actinomycosis have been disappointing. In no case has complete recovery resulted even when treatment was continued for many weeks. One case of cervical actinomycosis was given over fourteen million units in three courses. The sinus healed each time but subsequently recurred. A case of actinomycosis of the appendix received seven million units without improvement.

Treatment of Meniere's Syndrome

By J. J. RAINEY

(Abstracted from the *New York State Journal of Medicine*, Vol. XLV, 15th August, 1945, p. 1753)

No two cases of Ménière's syndrome are exactly alike. It is a relatively common condition but may be mistaken for something else. At first sight the symptom complex, vertigo and tinnitus based on nerve deafness, would seem easy to diagnose. However, there are considerable variations in the symptom complex. Some patients suffer from brief attacks of vertigo and nausea, while others suffer from constant unsteadiness and other concomitant symptoms, so much so that it is often difficult to decide just where the dividing line lies between the minor and major attacks. Moreover, the explosive character of the major attacks, with the patient thrown off balance, the resultant nausea and vomiting, the pallor, the sweating, and above all the terrified expression of the victim make the picture less of a blue print than one has been led to believe.

It is generally agreed that the symptoms of Ménière's syndrome are the result of a local disturbance of the inner ear caused by the release of histamine. It is well established that the intravenous use of histamine phosphate desensitizes the patient and brings about amelioration of the symptom complex. If this remedy had been used early in the treatment of the group of patients just described, it is quite certain that most of them would have had prompt relief (personal observations).

During the past four and a half years we treated 60 patients with histamine phosphate (the technique of the administration of which is described in a former paper). Fifty-three of these patients suffer from major attacks and the results in 49 cases were excellent. Seven patients had what we considered minor attacks of the syndrome. They carried on their usual occupations, but were subject to daily attacks of vertigo of very brief duration. Others had an ever-present feeling of instability. In this group 4 were men and 3 were women. Some of the patients said they felt better after treatment, but it is our impression that the treatment had no effect on the condition calling for relief, and that these patients, many of whom show the all-too-frequent irascibility of middle life, belong in the hands of the understanding family physician.

About 25 per cent of the major cases have a return of symptoms within four, eight, or more commonly twelve weeks. Most of these are given a second series of treatments, and on occasion a third series is given.

The procedure followed is to give a series of three intravenous treatments, the second treatment forty-eight hours after the first, and the third, the day following the second. The patient has breakfast before medication. Three patients responded badly when the treatment was almost completed. They become pale, the pulse was thready, and 2 vomited. The needle was withdrawn at once, and no further treatment was necessary for the complicating reaction. In those patients who reacted badly the subsequent dose was reduced to thirty drops per minute instead of the usual fifty or sixty drops per minute. None of those patients for whom the succeeding dose was reduced showed any untoward reactions. As many of the patients gain considerable weight and are inclined to indulge in rich food, they are put on a bland, soft, non-gaseous diet which seems to control some of the side symptoms of which they complain. We no longer use the so-called subcutaneous maintenance dose of histamine phosphate. It has proved to be without value except for its psychologic effect.

COMMENT

In appraising a new treatment one must not be led too far afield by apparently good results. It is questionable whether any patient ever had his hearing improved by administration of histamine or any other drug used to relieve Ménière's syndrome. With every

new advance in medicine, we may forget an old truth. It is often forgotten that nerve deafness may have an acute catarrhal deafness grafted upon it. Then if the catarrhal deafness disappears, the treatment of the moment receives credit for the improvement in hearing. One does not have to go farther than arthritis for another specific example. Tinnitus is improved in many instances, but again there may be a resurgence, now and then, of head noises. In a few cases, for some time following the treatment there are occasional attacks of vertigo of a few seconds or of a minute or two duration. Postural occupation is of importance. Farmers, during milking, and card players seem most affected. Dandy states that the syndrome lends itself to statistical conclusions. That is quite true. There can be no doubt that some of the patients reported in this paper as being apparently cured by histamine would have recovered spontaneously, but his statement holds good not only for medical treatment but also for surgical intervention.

CONCLUSION

The patient afflicted with Ménière's syndrome is best treated by a private physician rather than by a large clinic where there is a division of responsibility among the personnel. He should live within easy call of his doctor, for the therapy is only one step in the alleviation of his symptoms. Many of the victims of Ménière's syndrome live in constant fear of recurrent attacks and require assurance from their physicians.

If the physician's diagnosis of Ménière's syndrome is correct, he has at hand, in histamine phosphate used intravenously, a treatment that will give prompt relief in the majority of his cases. It is a simple treatment, relatively safe, and the only requirement for success is perseverance on the part of both physician and patient.

Cultivation of Malarial Parasites

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXVIII, 18th August, 1945, p. 1167)

A MUCH more successful *in vitro* cultivation of malarial parasites is now reported by Ball and his co-workers of Harvard Medical School. They selected the erythrocytic form of *Plasmodium knowlesi*, a malaria parasite of monkeys (*Macaca mulatta*), which also produces infection in man. This parasite has a twenty-four-hour asexual life cycle. They first developed a buffered nutrient fluid consisting of glucose (2.5 gm. per litre), proteose peptone (1.5 gm.), a purified mixture of amino acids (0.5 gm.) and the usual salts necessary for tissue cultures, supplemented by presumably optimal amounts of all known essential vitamins.

Two culture techniques were developed. By the first, or 'rocker dilution', technique 1 part of whole malarial blood was added to 3 parts of nutrient fluid, and the mixture was placed in a flask equipped with a gas inlet and outlet. The container was placed in a rocker machine, which just kept the red cells in suspension. A slow flow of 5 per cent carbon dioxide in 95 per cent air was passed through the container. The whole procedure was carried out with aseptic precautions at a temperature of 38.5°C. The best results were obtained when the number of parasitized cells in the mixture was not more than 25,000 per cubic millimetre. More highly parasitized blood was diluted with several times its volume of normal monkey blood.

The second, or 'rocker perfusion', technique employed a cellophane membrane to separate the infected blood from the nutrient medium. Several types of apparatus were developed. For small volumes of blood the cellophane membrane was stretched over one end of a glass tube about 1 inch in diameter. The blood was placed within the tube directly on the membrane. The tube was mounted in a vessel containing the nutrient fluid so that the membrane was just wet by the fluid. For larger cultures a coil of cellophane tubing was used. This was supported by a

glass form and immersed in the blood. Nutrient fluid was allowed to flow through the tubing at a rate of approximately 1 c.c. per minute. In both types of cultivation a slow stream of 5 per cent carbon dioxide in 95 per cent air was passed through the container, which was gently rocked to keep the corpuscles in suspension. All operations were performed at 38.5°C.

Cultivation was usually carried on for twenty-four hours. If subcultures were desired, a fresh set-up was made at the end of each twenty-four hours, the parasitized blood being diluted with normal blood and the nutrient fluid replaced. The addition of one-fourth volume of normal blood serum to the nutrient fluid was an advantage. In eighty-nine experiments the average increase in parasite count within twenty-four hours was approximately fourfold. In 60 monkeys the average *in vivo* increase in parasite count for the same period was also fourfold. Differential counts during the twenty-four-hour period showed that segmentation usually takes place between the fifth and the tenth hour.

Under the rocker perfusion technique six successive generations have thus far been cultivated by the Harvard pathologists. The infectivity of the sixth generation was demonstrated by inoculation into a monkey. The technique is now being applied with encouraging results to the *in vitro* cultivation of human malaria parasites.

Penicillin in Subacute Bacterial Endocarditis

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXVIII, 18th August, 1945, p. 1166)

FRIEDMAN, Hamburger and Katz suggested that continued deposition of new fibrin and platelets on the vegetations created an impenetrable barrier to the action of otherwise effective agents; they proposed that a patient with bacterial endocarditis be first subjected to treatment with an anticoagulant such as heparin. Loewe and Rosenblatt deposited the drug subcutaneously, utilizing the Pitkin menstruum, which is composed of gelatin, dextrose, glacial acetic acid and water in definite proportions. By this technique a slower and more equable absorption of heparin was accomplished. Loewe and his co-workers administered heparin and sulfonamide compounds combined to 17 patients with subacute bacterial endocarditis but could not determine an appreciable effect on the course of the disease in 15. Of the 54 patients treated with penicillin and heparin combined, 14 were failures and 40 appeared to be cured. In the latter group 37 are alive and many have resumed useful occupations; 3 have died of other causes. In the group of failures of treatment, 13 deaths followed circulatory failure, coronary occlusion, embolization and pneumonia. These authors feel that a five-week course of treatment with penicillin should be the standard minimum. Additional courses are well tolerated and are to be given when indicated. Based on penicillin sensitivity tests, an average daily dose of 200,000 Oxford units is suggested. Inadequate dosage invites failure, and the organisms may acquire resistance that is so high as to render future therapeutic levels unattainable. The total unitage in their series varied between the low 86,700 and a high of 48,930,000 Oxford units. To heparinize the blood effectually required subcutaneous deposition of 300 mg. of heparin every second or third day.

Dawson and Hunter administered combined heparin-penicillin therapy to 16 patients with bacterial endocarditis. The infection of 11 patients has apparently been terminated. These authors feel that patients with subacute bacterial endocarditis should be treated with penicillin if the infecting organism is a streptococcus sensitive to the action of the drug. They were impressed with the advantages of administering penicillin by continuous intramuscular drip, as advocated by Harris.

Bloomfield and his associates obtained excellent results from intensive penicillin therapy alone carried

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on for six to eight weeks. All 11 patients were promptly made-bacteria-free except 1, who died early in the course of treatment. These authors believe that the time factor is even more important than the daily dose. The failures of the early attempts were due to short periods of treatment. Continuous treatment over long periods is more likely to eradicate the infection than brief courses of penicillin.

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STUDIES ON MALARIA IN INFANTS IN NORTH KANARA DISTRICT, BOMBAY PRESIDENCY

The results of analysis of 1,628 blood examinations from infants in Haliyal and Yellapur in North Kanara District are presented.

There is a well-defined season of transmission in Haliyal from September to December, but in Yellapur this is prolonged throughout the year, except for the monsoon months of July to October.

P. vivax and *P. falciparum* are prevalent throughout the year in equal proportions. *P. malariae*, which in the previous year was more abundant, appears to have been suppressed during the year of study when transmission was more severe.

Both *P. vivax* and *P. falciparum* have a high relapse rate (33 per cent) in infancy; the concentration of parasites among infants is less than in children of 2 to 10 years of age, but they develop adequate gametocytes to play an important rôle in transmission.

There is a progressive increase in infection rates among infants with increasing age, but this is shown to be due to (a) the cumulative effect of a longer period of exposure and probably (b) a greater degree of exposure.

During the earlier phases of transmission, younger and older infants exhibit equal and high rates of infection. Towards the later phases, the older infants exhibit much higher rates. In the off-season, both groups exhibit low rates.

While a single examination at the height of transmission is adequate to assess the quantum of transmission and consequently the efficacy of control measures, provided it includes the same proportion of younger and older infants from year to year, repeated examinations are necessary to assess the season of transmission in general, and of species of plasmodia in particular.

There seems no evidence of any factor of immunity operating in any period of infancy, and this factor can

only be assessed by repeated examinations and making allowances for the period of exposure.

A special study has shown that the effects of malaria on infants would seem to consist in this area of (a) an increased number of still births and premature births, (b) increased neonatal mortality due to indirect effects of maternal malaria, and (c) increased mortality in the primary attack; infants who survive the primary attack do not appear to incur any special increase in the hazard of mortality due to malaria or any secondary cause.

INVESTIGATION OF LONG-TERM PERIODICITY IN THE INCIDENCE OF EPIDEMIC MALARIA IN THE PUNJAB

The curve of annual malaria mortality in the Punjab, as represented by each year's epidemic figure, has been studied over a period from 1867 to 1943. A statistically significant decrease over this period of 77 years has been demonstrated. Further, there is a strong indication that epidemics tend to occur after a period of about eight years. The mathematical methods that have been adopted to study the existence of this periodicity statistically have their limitations, inasmuch as they are designed to test periodicities of fixed duration, such as are generally noticed in physical phenomena. These methods do indicate the existence of eight-year cycles in the visitations of epidemic malaria in the Punjab. But in view of the period studied being not of a sufficiently long duration for the application of the statistical tests, and in view of the rigidity of the technique employed in testing it, the existence of the periodicity has not been conclusively established. For purposes of forecasting, however, it is suggested that due notice should be taken in future of the likelihood of occurrence of an epidemic after a period of eight years. In some cases this period may fall short by one year while in others the epidemic may be delayed by one year.

ON THE BIOLOGICS OF *A. culicifacies* GILES. PART II. THE ECOLOGY OF THE IMMATURE STAGES

A study of the ovipositing habits of *A. culicifacies* and a survey of natural breeding places showed that the gravid females deposit eggs at random and that they do not exercise any choice in the selection of their breeding places.

Oviposition usually took place at night, 60.1 per cent eggs being deposited in the first third of night, 27.9 per cent in the second third and 12 per cent in the last third. The average numbers of eggs laid during different seasons were more or less constant (115-134 eggs).

Females when afforded the choice of water at room temperature, i.e. 33°C. (90.4°F.), and water at a constant temperature of 42°C. (107.6°F.) showed a slight preference for cooler water. When exposed to a constant temperature of 45°C. (113°F.) the females were distinctly attracted to cooler water. Temperature seemed to play no part in the selection of the breeding places by the ovipositing females.

The development of eggs, larvae, and pupæ was followed at different constant temperatures 20°C. (68°F.) to 40°C. (104°F.). The most favourable range of temperature for the development of all stages of *A. culicifacies* was found to be 28°C. (82.4°F.) to 36°C. (96.8°F.), optimum being 32°C. (89.6°F.). The thermal death point of different stages were:—

Eggs	
Larvæ 1st instar	53.0°C. (127.4°F.)
" 2nd "	46.3°C. (115.3°F.)
" 3rd "	46.2°C. (115.1°F.)
" 4th "	45.5°C. (113.9°F.)
" "	45.5°C. (113.9°F.)

An extensive series of water temperature measurements in the field showed that in summer the maximum temperature in some of the breeding places was as high as 44.9°C. (112.8°F.); in these months the water temperature appears to be the limiting factor and *A. culicifacies* was observed to oviposit in wells and tanks. The gravid females laid their eggs indiscriminately up to 120 p.p.m. of saline and free ammonia;

A. subpictus and *A. annularis*, the two other common species, behaved in the same way. Larvæ of *A. culicifacies* and of the other two species, however, did not develop in concentrations of saline and free ammonia exceeding 12 parts per million.

A. culicifacies was found to be fairly sensitive to pollution by decaying vegetation. If this exceeded 1,064.5 p.p.m., eggs were not deposited and no further development of larvæ took place.

Shade itself had no appreciable influence on egg laying, but it exerted an inhibitory effect by causing mechanical obstruction to ovipositing females of *A. culicifacies*.

BEHAVIOUR OF *Anopheles fluviatilis*. PART III. LARVÆ HABITATS IN NORTH KANARA DISTRICT

Summarized data of an extensive series of anopheles larvæ collections totalling 9,526 positive searches made in North Kanara District in Bombay Province, between August 1942 to December 1944, are presented, with special reference to *A. fluviatilis*. While confirming the observations of previous workers that streams and channels are the preferred habitats of the species it has also been determined that ricefields, both fallow and growing, constitute important sources of this species.

HOUSE SPRAYING WITH D.D.T. AND WITH PYRETHRUM EXTRACT COMPARED: FIRST RESULTS

D.D.T. at the rate of 1 qt. 5 per cent solution per 1,000 sq. ft. will prevent infection in the *fluviatilis* group in a hyperendemic area, in the 'cold' weather of Southern India, for eight weeks. It acts by reducing density as well as longevity.

Pyrethrum spraying, 6 days each week, reduces density and longevity sufficiently to inhibit gland infections. The density reduction is much less than with D.D.T. This is probably due to a certain proportion of the house population leaving before the morning pyrethrum spraying, whereas with D.D.T. it is believed that any specimen which has rested after feeding on a still active treated surface must die.

Pyrethrum spraying, twice a week at $\frac{1-1.1}{2-3}$, has no effective result either on density or on infectivity. As a method of protecting a population exposed to the *fluviatilis* group it is useless. Here it only served to improve the standard of protection afforded to the railway population by preventing the infiltration into the colony of specimens infected in the village.

Assuming the cost of D.D.T. as stated to be correct, over the two months December to February, a period of heavy though not of maximal transmission, D.D.T. is 20 to 25 times cheaper *per capita* per week than pyrethrum.

DETAILS OF THE PROCEDURE ADOPTED IN MAINTAINING A LABORATORY COLONY OF *A. fluviatilis*

The following is a summary of this article:

In January 1941, a colony of *A. fluviatilis* was established at Mettupalaiyam, a town 17 miles east of Coonoor about 1,000 feet above sea level. This has now been maintained for more than a year and appears to be in a vigorous condition. The colony was started from the eggs laid by wild-caught females which, when gravid, were isolated in individual tubes. Details regarding isolation, rearing of larvæ, care of the pupæ, care of the adults, mating and fertilization of the females, and the special precautions taken are given.

MALARIA TRANSMISSION IN AND AROUND VIZAGAPATAM

This paper records observations carried out from September 1942 to October 1944. Malaria incidence in and around Vizagapatam is normally low, with spleen rates less than 10 per cent, but localized epidemics of varying severity occur from time to time.

Previous investigations.—Gut infection of *A. culicifacies* were recorded by Krishnan (1925), one out of 31 dissected, and by King and Venkataraman (1929), 3 out of 189.

Senior White and Venkat Rao, summarizing their work from 1936 onwards, recorded a single specimen of

A. culicifacies infected (both gut and gland) out of 6,608 dissected. The infected specimen was caught in a human bait trap. The sporozoite rate in *A. varuna* was 0.017 per cent and in *A. stephensi* var. *mysorensis* 1.75 per cent. They concluded that the last-named was the principal rural vector in this area and that *A. culicifacies* played no part of any practical importance in transmission. Measures for the control of this species in the railway area around Vizagapatam had been omitted since 1937 with no apparent ill effect on malarial incidence (Senior White and Venkat Rao, 1943).

Data now recorded.—The following species of Anopheles were encountered:

annularis, *barbistrostris*, *culicifacies*, *hyrcanus*, *karwari*, *maculatus*, *moghulensis*, *pallidus*, *stephensi*, *subpictus*, *tessellatus*, *theobaldi*, *vagus* and *varuna*.

A malaria epidemic occurred in 1942 during which the authors recorded 1 gland infection in *A. stephensi* (race not determined) out of 165 dissected and 1 gut infection out of 395 *A. culicifacies* dissected in a village near Vizagapatam. In the town itself 1 gut infection in *A. stephensi* was observed out of 52 dissected in September, 7 gland infections out of 139 in October, 2 gland infections out of 37 in November and 1 gland infection out of 48 in December. One gland infection was recorded out of 43 *A. culicifacies* dissected in October and 1 out of 128 in November.

In the rural area the principal breeding places of *A. stephensi* were in seepage outcrops in nullahs, and in the urban area pukka wells and artificial containers. Adults were rare in pukka houses, but plentiful in thatched huts and cattlesheds. Out of 11 infected specimens collected in the urban area, only 1 (a gut infection) was caught in a house, 5 (all gland infections) in huts occupied both by human beings and cattle. In rural areas adults were observed resting at dawn in the thatched verandahs or under the projecting eaves of huts.

The total number of *A. stephensi* dissected from September 1942 to October 1944 was 692, of which 388 were collected in the town of Vizagapatam and 304 in the rural area. In the urban area the oöcyst rate was 0.26 per cent and the sporozoite rate 2.6 per cent, the corresponding rates in the rural area being 1.3 per cent and 1.3 per cent respectively. Infections were noted in every month from September to May inclusive. Out of 11 infected specimens in which the race was determined from measurements of the eggs deposited, 6 out of 7 from the town were classed as type (B) and 3 out of 4 from rural areas as var. *mysorensis* (M). The infection index per cent for B was 6.9 and for M 4.8, the sporozoite indices being 6.9 and 2.4 respectively. The authors conclude that both races are efficient malaria carriers and have been responsible for epidemic outbreaks in both urban and rural areas, var. *mysorensis* predominating in the rural and the type form in the urban area.

The infection rate in *A. culicifacies* was 0.48 per cent and the sporozoite rate 0.19 per cent, infections being recorded in August, October and November. The infection rate in this species in the urban area (844 dissections, 1 gut and 2 glands) was 0.355 per cent and the sporozoite rate 0.237. In the rural area (8,143 dissections) 1 gut infection was recorded out of 510 collected in one locality (Saripalli), the remaining 7,633 yielding negative results. In a footnote it is stated that one additional gland infection was observed out of 234 dissected in January 1945.

The authors conclude that *A. culicifacies* plays a definite, though possibly a secondary, rôle in transmission of malaria in and around Vizagapatam 'especially in conditions favourable for epidemic incidence'.

MALARIA SURVEY OF SALSETTE ISLAND

This paper records a report on malaria survey carried out in July-August and October-November 1943. Malaria is prevalent in hyperendemic form in the central hill and foothill region with a spleen rate of over 50 per cent, and tails off to moderate endemicity over a region located about 2 miles from the hills and

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their spurs. The coastal strip to the east, being narrow and mostly within 2 miles of the foothills, is moderately endemic with a definite seasonal rise from September to November. The spleen rates have a sharp seasonal rise (up to 20 per cent) and on account of a good recovery rate, mainly due to treatment, show no evidence of endemicity in the off-season (less than 10 per cent). The parasite rates show a far greater seasonal swing (up to 50 per cent) and give a truer picture of the seasonal hazard than the spleen rates. During the season, *P. falciparum* is predominant and the gametocyte rate is high. There is no evidence of regional epidemics attended with a high mortality, but exacerbations occur from year to year, mainly due to variations in the distribution rather than the amount of rainfall, pointing to a stream breeder as the probable vector. The coastal towns and villages to the west of the hills are more than 2 miles away in several places and show no evidence of malarial endemicity even during the season. Malaria cases occurring in this region are mainly imported, while in the hills and to their east the disease is autochthonous and indigenous. The vector species is *A. fluviatilis*, with a total infection rate of 8.4 per cent during the season (16 out of 191, positive for either oöcysts or sporozoites). Other species are not considered of importance in malaria transmission. *A. fluviatilis* breeds principally in hill streams and channels flowing down the slopes of the hill past the coastal strips on either side and eventually into the creeks. These are liable to flushing during the monsoon and hence breaks in the monsoon increase the hazard of transmission. While the hills and foothills are everywhere dangerous, foci of different degrees of malarial prevalence are found in the coastal strips, mainly depending upon their proximity to the hills or to the streams arising from them. A distance of about a mile sometimes makes a great difference in the degree of malarial endemicity. Although *A. fluviatilis* is relatively sparse in the coastal areas to the east of the hills, the exclusive preference of this species for human blood and its high vectorial capacity account for the sharp seasonal swing in the incidence of malaria. On the top of the hills and foothills, although *A. fluviatilis* shows marked seasonal variations, it is found in sufficient numbers to account for hyperendemicity and a poor recovery rate during the off-season.

MALARIA IN PANDHARPUR, BOMBAY PRESIDENCY

A malaria survey of the town of Pandharpur, a pilgrim centre located 265 miles south-east of Bombay in the District of Sholapur, Deccan, at a height of 1,500 feet above sea level, was carried out during the period September 1937 to May 1938. The spleen rate in the railway colony, where regular treatment is provided, was 15 per cent. Generally speaking, the urban rates were extremely low, but a figure of 22 per cent was recorded in one quarter of the town and of 33 per cent in another.

The chief sources of anopheline breeding were the river bed, the margin of a large tank and leakages from the irrigation system emanating from it, quarry-pits and rainwater collections.

The species of Anopheles found were:—*annularis*, *barbirostris*, *fluviatilis* (one specimen only), *hyrcanus* var. *nigerrimus*, *karwari*, *pallidus*, *stephensi*, *subpictus*, *tessellatus*, *theobaldi*, *turkhudi* and *vagus*.

The only species found infected was *A. culicifacies*, oöcysts being observed in one specimen out of 206 dissected in December.

From the evidence available it is surmised that malaria transmission commences with the advent of the monsoon in June and continues until the end of the year.

The anti-malaria measures adopted included minor levelling and drainage operations, the application of larvicides to breeding places, and the spraying of habitations with pyrethrum insecticide.

Cross Immunity Between Four Strains of Tsutsugamushi Disease (Scrub Typhus)

By N. H. TOPPING

(Abstracted from the *Public Health Reports*, Vol. LX, 17th August, 1945, p. 945)

Cross-immunity tests have been done in guinea-pigs with four separate strains of tsutsugamushi disease virus. Two of the strains, Karp and case No. 9, were from the New Guinea area, the Seerangayee strain was from Malaya, and the Gilliam from the Assam-Burma border. These four strains were selected for their wide geographic distribution. All four strains were well adapted to guinea-pigs and were being passed by intraperitoneal inoculations of a liver and spleen suspension (approximately 10 per cent). The Seerangayee strain has a high fatality rate and, in order to have a sufficient number of recovered animals from this strain, it was necessary to inoculate guinea-pigs subcutaneously. The cross-immunity tests were done by inoculating recovered guinea-pigs intraperitoneally with one of the heterologous strains.

It is clear from the results of these tests that cross-immunity exists in guinea-pigs between these four strains of tsutsugamushi disease. The only differences observed in the strains were fatality rates in guinea-pigs, the Seerangayee having the highest rate and case No. 9 the lowest, with the Karp and the Gilliam intermediate. The results do not necessarily mean that these four strains are immunologically identical. As an example, cross immunity exists between epidemic and murine typhus yet by other immunological procedures they have been shown to be distinct.

Reviews

PRINCIPLES OF HUMAN PHYSIOLOGY (STARLING).
—By C. Lovatt Evans, D.Sc., F.R.C.P., F.R.S.
Ninth Edition. 1945. J. and A. Churchill, Ltd., London. Pp. x plus 1155, with 668 illustrations. Price, 36s.

THIS is the ninth edition of this book, of which the reviewer remembers well the earlier editions, and the contrast is interesting. As the editor writes in the preface 'It is this reciprocal reaction between the whole and the part that is brought out in the modern development of physiology. . . . Yet the contemplation of the functions of the several parts remains as important,

by furnishing elements for a synthesis, as ever it was. It is in the presentation of the varying functions of the various parts of the body and the building up of this synthesis that the strength of books such as this lies, but as the editor states there are still some important gaps to be filled.

In this edition, a new feature is short sections of historical notes which are inserted at suitable places in the book. Some of the historical ideas on physiology seem to us to be laughable now, but, as the editor states, it is probable that the reasoning powers of man have remained much the same throughout the centuries, and when we feel disposed to smile,

we should not forget that with the same data we should have done no better.

One chapter, on the temperature and heat balance of the body, is entirely new, but several other parts of the book have been rewritten, and some new illustrations have been added. The book remains one of the most excellent of its kind.

MEDICAL JURISPRUDENCE AND TOXICOLOGY.—

By John Glaister, J.P., D.Sc., M.D., F.R.S. (Ed.). Eighth Edition. 1945. E. and S. Livingstone Limited, Edinburgh. Pp. xii plus 691, with 222 illustrations; 89 in colour. Price, 30s.; postage, 8d. (home)

THIS standard work has been revised and brought up to date in this edition. New matter is included on such subjects as immersion foot, crush injury, the Rh factor in blood, etc. A considerable amount of new material has been added in relation to asphyxial deaths, identification of firearms and projectiles, states of insensibility and other subjects. Some new poisons have been added to the toxicological section. The number of illustrations have been substantially increased. These, together with the illustrative cases, add to the value of the work as a reliable guide to forensic medicine. In treatment of snake-bite, local application of potassium permanganate has been advocated and suction of the wound regarded useless; this may not be acceptable to all.

R. N. C.

RECENT ADVANCES IN NEUROLOGY AND NEURO-PSYCHIATRY.—By W. Russell Brain, M.A., D.M. (Oxon.), F.R.C.P., and E. B. Strauss, M.A., D.M. (Oxon.), F.R.C.P. Fifth Edition. 1945. J. and A. Churchill Limited, London. Pp. xiv plus 363, with 32 illustrations. Price, 18s.

IN this edition, the title of the book has been changed from the old one, 'Recent Advances in Neurology', because, as the authors rightly point out in the preface, there is a vast field in which neurology and psychiatry overlap and which may conveniently be designated as 'neuro-psychiatry'. In recent years, the subject has made great progress in certain fields due to the development of knowledge and methods of investigation and treatment, consequently the book has been almost entirely rewritten. New topics include electrical convulsant therapy for mental disorder, prefrontal leucotomy, peripheral nerve injuries, vaso-neuropathy after chilling (immersion foot and hand), etc. Among the new forms of treatment are described penicillin for meningitis and thymectomy for myasthenia gravis. The chapter on electro-encephalography has been much enlarged and covers its applications to neurophysiology, sleep, epilepsy, the psychopathies and psychoses. Much new material has been added on the vitamin deficiencies, vertigo, sciatica, etc., and there is a chapter written by Douglas Northfield on the treatment of head injuries from the surgical standpoint. The book is a valuable compendium on neuro-psychiatry and fulfils the intention of the authors, expressed in their first edition, that the subjects treated should have a clinical bearing.

R. N. C.

A TREATISE ON HYGIENE AND PUBLIC HEALTH.—

By B. N. Ghosh, M.B.E., F.R.F.P.S. (Glas.), F.R.S. (Edin.). Eleventh Edition. 1945. Scientific Publishing Company, Calcutta. Pp. xvi plus 707, with 161 illustrations. Price, 21s.

IN this edition of this book which deals with the subject with special reference to the tropics, and with India in particular, the preface states that 'since the whole book had to be reset efforts have been made to make such changes as were found necessary in view of the experience accumulated mainly as a result of war conditions'. Also in accordance with the changing conception and outlook on public health, there is now a new chapter on Social Medicine written by Dr. J. B. Grant, C.B.E., Director of the All-India Institute of Hygiene and Public Health. Another new chapter is

on Camp Sanitation; based upon 'Field Service Hygiene Notes'. This edition, as the previous editions, should be very useful to medical men and public health administrators in India. The book is well printed and bound and its price moderate.

R. N. C.

ILLUSTRATIONS OF BANDAGING AND FIRST-AID.

—By Lois Oakes, S.R.N., D.N. Third Edition. 1944. E. and S. Livingstone Limited, Edinburgh. Pp. vii plus 272, with over 300 illustrations. Price, 6s. net

THE aim of this book is, as stated in the preface, 'to enable the student, by means of pictures, to master quickly the science and art of bandaging and of first-aid in fractures and hæmorrhages'. That the book has eminently succeeded in this respect is evident from the fact that three editions, in addition to a cheap one and one in Spanish, have come out within four years. The present edition consists of six sections of illustrations—triangular bandaging, roller bandaging, shock, first-aid in hæmorrhage, first-aid in fractures, and blanketing a stretcher and removal of patient; there is also a supplement of coloured illustrations of war wounds. The book is a valuable guide for students and first-aiders.

R. N. C.

PRACTICAL BANDAGING.—By Eldridge L. Ellason, A.B., M.D., Sc.D., F.A.C.S., F.I.C.S. Sixth Edition. 1943. J. B. Lippincott Company, London. Pp. x plus 128, with 150 illustrations. Price, 10s. 6d.

THIS edition, like its predecessors, thoroughly covers the field and deals with the newer woven bandages and adhesive materials as well as the more rigid, hardening bandages. The 150 illustrations contained in the book, both photographs and drawings, have been made as correct as possible and will make realistic and lasting impressions on students and nurses for whom the book is intended.

R. N. C.

AIDS TO ORTHOPÆDIC SURGERY AND FRACTURES.—By I. E. Zieve, M.A., F.R.C.S. Second Edition. 1944. Pp. iv plus 270. Baillière, Tindall and Cox, London. Price, 6s.

AIDS TO MATERIA MEDICA.—By G. H. Newns, M.D., M.R.C.P. Third Edition. 1944. Pp. vii plus 211. Baillière, Tindall and Cox, London. Price, 5s.

THESE two pocket books belong to the Students' Aid Series published by Baillière, Tindall and Cox. This series is compiled with the object of assisting students preparing for their examinations in the different subjects. In the editions under review, considerable transposition of sections has been made, and the books brought up to date. Both the books are based on standard works on the subject and the facts given are accurate and concise.

SURGERY OF MODERN WARFARE.—Edited by Hamilton Bailey, F.R.C.S. Six Parts. Third Edition. 1944. Pp. xvi plus 1108, with 1,128 illustrations, many in colour. E. and S. Livingstone Limited, Edinburgh. Price, 15s. net each part

A TEAM of 76 contributors 'who can claim to represent British Surgery' have contributed to this set of six volumes, and the editor states in the preface that 'reflected in its pages is teaching from London, the Provinces, Scotland, Wales and Ireland, and experiences culled from the Navy, Army, Air Force and Emergency Medical Service'. Some of the contributions are based on the experiences in the present war, some on those of the war of 1914-18, and some compare and contrast the surgery of both campaigns.

Part I contains two sections, one on wounds; general considerations, and the other on the general condition of the casualty and his resuscitation. In part II there are five sections under the following titles: frost-bite; burns and skin grafting; anæsthetizing the wounded; wounds, general operative considerations;

wounds, special infections; wounds, special considerations. Part III contains three sections on wounds of blood vessels, methods of immobilizing the limbs, and amputations. There are four sections in part IV, on wounds of bones and joints, of the hand and foot, of tendons and peripheral nerve injuries, and of the spine; it also contains two out of three chapters of the section on wounds of the head and neck. Part V contains the third chapter of 'wounds of the head and neck', two sections on otorhinolaryngology in relation to war injuries, and wounds of the eye and orbit, and also five out of 12 chapters of the section on wounds of the trunk. The remaining chapters of the section on wounds of the trunk, a section on surgical diseases encountered in sub-tropical countries, one on administration, and an appendix are contained in part VI.

The book is intended to provide guidance on the special technique and management of the wounded for the trained surgeon who has to deal with the injuries associated with warfare. It represents a magnificent attempt at providing a *vade mecum* in all spheres of surgical activity connected with war injuries. The illustrations are more in number than the pages themselves, most of them containing such a wealth of colour and attention to detail that the reader cannot fail to notice the desired information. The set was first published in 1941. In the present third edition, scarcely any section has been left unrevised and obviously no effort has been spared by the editor, contributors, printers and publishers. The book embodies only the best and most modern practice, and although the war is past, we have no doubt that the utility of the book will long endure. A book to be strongly recommended.

AIDS TO THEATRE TECHNIQUE.—By Marjorie Houghton, S.R.N., S.C.M., D.N., and Margaret Harding, S.R.C.N., S.R.N., S.C.M. 1944. Pp. xiii plus 262, with more than 100 illustrations. Baillière, Tindall and Cox, London. Price, 4s.

This is one of the Nurses' Aids Series published with the object of providing 'in condensed but easily readable form extensive and comprehensive information on each particular subject'.

In the first five chapters brief descriptions are given of the theatre unit, the operation table including the position of the patient for various operations, the theatre nurse and her duties, sterilization, and anaesthetics. The sixth chapter gives short notes on technical terms, and the next chapter describes general instruments, ligatures and sutures. The remaining thirteen chapters provide lists of instruments for the various common operations which may be considered standard. A glossary of instruments is given in the final chapter. There are plenty of good illustrations.

The authors are sister-tutors in well-known teaching hospitals, and they have also secured the collaboration of expert medical men on the subjects. The book is a very useful one for nurses.

TREATMENT BY MANIPULATION.—By A. G. Timbrell Fisher, M.C., M.B., Ch.B., F.R.C.S. Fourth Edition. 1944. Pp. viii plus 224, with 81 illustrations. H. K. Lewis and Co., Ltd., London. Price, 16s. net

MANIPULATIVE treatment has aroused great interest in recent times, and the author of this widely appreciated book was one of those who were instrumental in arousing this interest. The author's object in writing this book was to draw the attention to the value of this treatment 'in carefully selected cases, of certain of the sequelæ of injuries and diseases particularly affecting the joints, muscles, tendons and fasciæ', concerning which the author thinks that the literature is scanty. The book does not deal with 'setting' of fractures, the treatment of dislocations, and such other surgical procedures.

The first chapter gives a brief historical introduction to the subject mentioning the work of Hippocrates, John Hunter, John Hilton, H. O. Thomas, Sir James Paget, and Wharton Hood. In chapter II the pathology of the cases that may be cured or benefited by

manipulation is described under the following headings: articular or peri-articular adhesions; functional (hysterical) conditions of joints; subluxations and dislocations of joints, tendons, or intra-articular discs and adhesions in connection with muscles, tendons, and fasciæ. The third chapter deals with the prevention of adhesions, and the fourth is a short one on the diagnosis of adhesions. The next five chapters are on the general principles of treatment, and the treatment of the lower and upper extremities, spine and the sacro-iliac joint. The last three chapters are on the cult of osteopathy, the dangers of manipulation in unsuitable cases, and after-treatment. The printing and illustrations are good.

PHYSICAL TREATMENT BY MOVEMENT, MANIPULATION AND MASSAGE.—By James B. Menell M.A., M.D., B.C. Fifth Edition. 1945. Pp. x plus 512, with 288 illustrations, some in colour. J. and A. Churchill Ltd., London. Price, 30s.

THE fourth edition of this well-known book was reviewed in this journal in 1940. The present edition has been revised, and some additions and alterations have been made, particularly in the illustrations. The book has been written with two objects in view, to point out to practising masseurs, the 'rationale' of massage treatment, and to place in the hands of the medical profession a book to which they can refer when issuing instructions to their masseurs; it devotes much space to the personal attributes desirable in those who undertake massage work. It is thus an attempt to deal exhaustively with the subject, both from theoretical and practical points of view, and with every condition in which this kind of treatment may be indicated including neurasthenia, asthma, and adenoids. The present edition fulfils in a great measure the author's objects.

OUTLINES OF PHYSICAL METHODS IN MEDICINE.—By G. D. Kersley, M.A., M.D. (Cantab.), F.R.C.P. (Lond.). 1945. William Heinemann Medical Books, Ltd., London. Pp. viii plus 85. Price, 6s. net

THIS small book is based on the author's notes for the use of medical officers undergoing training and apprenticeship in physical medicine, and for revisionary courses for R.A.M.C. masseurs previous to trade testing. It contains eight chapters. The largest chapter, on movement and principles of remedial exercises, is given 24 pages, and the next big chapter is on electrotherapy consisting of 19 pages. The remaining six chapters, each of less than ten pages, are on the scope of physical medicine, heliotherapy, roentgen and radiotherapy; massage; hydrotherapy; and occupational therapy. The descriptions of methods given are concise, giving the main uses and contra-indications. There are also five appendices on a general craft analysis, a detailed analysis, crafts for specific conditions, staff and apparatus of a physiotherapy department, and of a complete rehabilitation department. The book, whose author has extensive experience in the subject, should be of value to medical practitioners and physiotherapists.

A TEXTBOOK OF PSYCHIATRY.—By D. K. Henderson, M.D., F.R.F.P.S., F.R.C.P.E., and R. D. Gillespie, M.D., F.R.C.P., D.P.M. Sixth Edition. 1944. Pp. xii plus 719. Oxford University Press, London

THE aim of these two authorities in writing this textbook in the English language on the subject, is stated in the preface to be 'to present psychiatry as a living subject, with important relations not only to general medicine, but to the social problems of everyday life'. A perusal of the book shows that they have carried out this aim in an admirable manner. The book reflects throughout its pages the biological hypothesis of Adolf Meyer which 'regards mental illness as the cumulative result of unhealthy reactions of the

individual mind to its environment', and in accordance with the modern 'dynamic' view, the authors have quoted clinical records of cases rather extensively from their own practice.

The first six chapters deal with the preliminary aspects of the subject. Chapter I gives a historical review of the care and treatment of mental illness from ancient times through periods of humane reform, abolition of restraint, hospitalization, up to the present 'social or community period'. Chapter II is on classifications and discusses the subject under psychological, physiological, ætiological, and symptomatological headings, quoting the British and American classifications. The authors also suggest a scheme of classification, and discuss future development. Chapter III deals with ætiology in detail (55 pages). The next three chapters are on method of examination, symptomatology, and general psychopathology, each about twenty pages.

Chapter VII, describing the psychoneurotic reaction types, is the second biggest chapter in the book. Affective reaction types are described in the next two chapters, one on manic-depressive psychoses and the other on involutional melancholia. Chapter X deals with schizophrenic reaction types, and the next chapter with paranoia, paraphrenia and paranoid reaction types.

Chapter XII is a short one on psychopathic states, and chapter XIII on special methods of psychical treatment.

Chapter XIV, the largest chapter in the book (105 pages), is devoted to the organic reaction types. It is followed by two short chapters on epilepsy and mental defect.

There is also a short chapter on psychoses and psychoneurosis in war. A fairly big chapter deals with the psychiatry of childhood. The last two chapters are on occupational therapy and the relations of psychiatry and law.

In the present edition, necessary additions and alterations to bring the book up to date have been made.

PSYCHOLOGICAL MEDICINE: A SHORT INTRODUCTION TO PSYCHIATRY.—By Desmond Curran, M.B., F.R.C.P., D.P.M., and Eric Guttman, M.D., M.R.C.P. Second Edition. 1945. Pp. viii plus 246, with 20 illustrations. E. and S. Livingstone, Edinburgh. Price, 10s. 6d. net

This book is what it claims to be, a short introduction to psychiatry, designed primarily for medical students and for others approaching the subject for the first time.

The introductory chapter brings out the importance of the subject to the medical student, quotes relevant statistics for Great Britain, and also an excellent statement of Wilfred Trotter. Then follow thirteen chapters the titles of which are: ætiology of mental disorder, symptoms in mental disease, psychiatric case-taking, treatment, constitutional anomalies, organic syndromes, psychiatric aspects of head injury, drug addictions, schizophrenia, the affective reaction types, obsessional states, hysterical reactions, and the legal aspects of mental illness. The authors have stressed the clinical aspect of the subject throughout the book. The appendix on psychiatry associated with war conditions contains four chapters entitled general principles, the examination of service patients, clinical syndromes, and management and treatment. Classified references for further reading, together with brief indications of the scope of the books, are given at the end. The book also contains 20 illustrations, a feature not often seen in books on this subject.

The second edition of this excellent primer, incorporating extensive revision and rewriting, is therefore to be much welcomed.

AIDS TO PSYCHIATRY.—By W. S. Dawson, M.A., M.D. (Oxon.), F.R.C.P. (Lond.), F.R.A.C.P., D.P.M. Fifth Edition. 1944. Pp. viii plus 306. Baillière, Tindall and Cox, London. Price, 6s.

This little book belongs to the 'Students Aids Series' published by Baillière, Tindall and Cox. The

fourth edition was reviewed in this journal in 1940. As pointed out in the previous review, the book is particularly devised to help students preparing for the D.P.M. examination. In the present edition, many sections have been rewritten and extensive revision has been carried out to bring it up to date.

AN INTRODUCTION TO PHYSICAL METHODS OF TREATMENT IN PSYCHIATRY.—By William Sargant, M.A., M.B. (Cantab.), M.R.C.P., D.P.M., and Elliot Slater, M.A., M.D. (Cantab.), M.R.C.P., D.P.M. 1944. Pp. xii plus 171. E. and S. Livingstone, Ltd., Edinburgh. Price, 8s. 6d. net

The authors state in the preface that the principles and techniques forming the subject-matter of this book have been tested 'in the hard school of work under pressure and on the largest scale' in one of the two evacuation centres of the Maudsley Hospital, and that only those subjects, of which direct clinical study on a fair scale was made, are included.

In the introductory chapter, the therapeutic aspects of psychiatry are discussed under two headings, the constitutional approach, and 'towards a rational therapy'. Then follow ten chapters on the insulin treatment of schizophrenia; modified insulin therapy; convulsion therapy; the treatment of cerebral dysrhythmia; chemical sedation and stimulation; continuous sleep treatment; some special uses of intravenous barbiturates; diet, vitamins and endocrines; prefrontal leucotomy; and the malarial treatment of general paralysis. Each chapter contains concise statements on such topics as history, selection of patients, risks and contra-indications, technique, clinical changes produced by treatment, results (statistically analysed when possible), follow-up, etc. The final chapter on the relation of psychological to somatic treatment discusses briefly the value of psychotherapy and points out the limitations to the physical approach. The book is written in a clear and easy style and embodies much valuable information on this wide and difficult subject which 'is now at a critical stage in its development'.

THE JOURNAL OF MENTAL SCIENCE. NO. 378. SPECIAL ISSUE. RECENT PROGRESS IN PSYCHIATRY.—Managing Editor G. W. T. H. Fleming. 1944. Pp. 509. J. and A. Churchill Ltd., London. Price, 30s. net

This book is a special issue of the Journal of Mental Science, published under the authority of the Royal Medico-psychological Association. It is a review of the work published during the five-year period from 1938 to 1942 approximately. It contains twenty-eight articles on different aspects of psychiatry, each written by a distinguished specialist in the subject. The managing editor contributes the introduction, and the article on prefrontal leucotomy. Four other members of the editorial board, F. L. Golla, Lionel S. Penrose, A. A. W. Petrie, and E. T. O. Slater, each contribute one article, viz, physiological psychology, mental defect, mental health services—present and future, and genetics in psychiatry. The remaining twenty-two articles with their respective authors are listed below: the anatomy of the nervous system by W. E. Le Gros Clark; electroencephalography by W. Grey Walter; biochemistry of the nervous system by Derek Richter; vitamin deficiency and the psychoses by W. Alex Caldwell; neuro-endocrine relationship by M. Reiss; mental testing by M. B. Brody; psychopathology by S. M. Coleman; neuropathology by A. Meyer; schizophrenia and arteriosclerotic, senile and presenile psychoses by W. Meyer Gross; depression by Aubrey Lewis; psychopathic personality by Desmond Curran; the psychoneuroses by W. H. Gillespie; psychotherapy by H. Crichton-Miller; psychiatric aspects of head injury by E. Guttman; neurosyphilis and its treatment by W. D. Nicol; child psychiatry by E. M. Creak; delinquency and crime by W. Norwood East; endocrinology in clinical psychiatry by R. E. Hemphill; convulsion therapy by L. C. Cook; insulin therapy by Thos.

[Dec., 1945]

Tennent; and legal aspects of psychiatry by P. K. McCowan. Thus practically all the important aspects of this wide and complicated subject, on which work has been done during the period under review, have been covered. Each article concludes with a comprehensive bibliography. The book provides much information on recent work, indispensable to psychiatrists.

A MANUAL OF TUBERCULOSIS: CLINICAL AND ADMINISTRATIVE.—By E. Ashworth Underwood, M.A., B.Sc., M.D., D.P.H. Third Edition. 1945. E. and S. Livingstone Ltd., Edinburgh. Pp. xvi plus 524, with 88 illustrations. Price, 15s. net

The title and sub-title of this book gives an indication of its scope. The author, as chief administrative tuberculosis officer of Westhand, has a first-hand knowledge of the problem from clinical and administrative aspects, and in this new edition, as he states in the preface, 'the needs of those who approach the subject of tuberculosis work as something more than a mere item in a course on clinical medicine have been borne in mind'. Among the twenty-four chapters it is good to see chapters on the evolution of pulmonary tuberculosis, the mental aspects of tuberculosis, the domiciliary management of tuberculosis, the post-sanatorium regime, the epidemiology of tuberculosis, administrative measures, the epidemiology of tuberculosis, tuberculosis and social medicine, and tuberculosis and war. In addition, of course, there are numerous chapters devoted to the more directly clinical aspects of tuberculosis.

The presentation of the subject is very simple and clear, but sufficient detail is given to make the presentation reasonably complete. It is apparently expected that some lay tuberculosis workers will study this book, and for them a glossary of technical terms is given at the end. A few medical men, however, will read this glossary with profit and the reviewer found there several terms of which he did not know the meaning. The book ends with a list of books recommended for further study. This book can certainly be strongly recommended. It is very well printed in large type on imitation art paper and it contains eighty-eight excellent illustrations. The price of the book is very reasonable.

CHEST SURGERY FOR NURSES.—By J. Lelgh Collis, B.Sc., M.D., F.R.C.S. 1944. Pp. viii plus 128, with 97 illustrations, 14 plates. Baillière, Tindall and Cox, London. Price, 7s. 6d. net

This small handbook attempts 'to present the more common points in the study of chest surgery for the benefit of the nursing staff treating such cases'. It is divided into two sections. The first section on anatomy and physiology contains a chapter on the anatomy of the chest, and one on the physiology and mechanics of the chest. The second section on the pathological conditions and their treatment begins with a chapter on general clinical principles and contains five more chapters on the pathological conditions of the chest wall, pleura, lung, mediastinum, heart and pericardium, diaphragm, and vessels. In the preparation of this book the author has collaborated with a nursing sister experienced in surgical chest cases, and the text matter is presented with clarity and without undue complexity. The illustrations are good.

SURGICAL NURSING AND AFTER TREATMENT.—By H. C. Rutherford Darling, M.D., M.S., F.R.C.S., F.R.F.P.S. Eighth Edition. 1944. Pp. x plus 686, with 210 illustrations. J. and A. Churchill Ltd., London. Price, 12s. 6d.

This excellent treatise on surgical nursing has been written in accordance with the syllabus for the final examination of the Australasian Trained Nurses Association. The seventh edition of this book was reviewed in this journal in 1942. In the present edition the book has been revised and brought up to date. We

may repeat the opinion expressed in our last review that 'a book of this type is invaluable for it enables the medical student, as well as the nurse, to understand fully certain apparently simple matters which are only too often barely mentioned in the textbooks'.

INDUSTRIAL NURSING: ITS AIMS AND PRACTICE.—By A. B. Dowson-Welsskopf, S.R.N. 1944. Pp. vii plus 159. Edward Arnold and Co., London. Price, 5s. net

As the title of this indicates, and as the author states in the introduction, the purpose of this book 'is to give an account of the practice of industrial nursing, indicating how this varies from institutional nursing and how a health department may be organized and maintained'.

The industrial nursing service is a comparatively new field. Its history and expansion, the training, recruitment and attributes of the industrial nurse, the scope and conditions of service of the industrial nurse, and the relations of the nurse with the factory personnel are explained in detail in the introduction and first two chapters. The actual duties of the industrial nurse are explained in the next eight chapters, of which 'the adolescent in industry' is a notable one. Appendix I gives a specimen 'standing orders' which should govern all routine treatment and deal with the reference of patients for medical advice. In appendix II details of the industrial nursing courses are given. The author writes from her own experience and has presented the subject in an interesting and informative manner.

Abstracts from Reports

ANNUAL REPORT OF THE SOUTH AFRICAN INSTITUTE FOR MEDICAL RESEARCH, JOHANNESBURG, FOR THE YEAR ENDED 31ST DECEMBER, 1944

The activities of the Institute were wide and varied. Only a few of these are mentioned here.

1. *War work.*—The production of typhus vaccine was well over two million doses, most of which were sent to Russia. Two methods were used, viz egg culture and gerbille culture. Both yield vaccine with a high rickettsial content. The manufacture of a crude penicillin filtrate was begun when the supply of the pure drug was short. It has poor keeping qualities, and its production will be discontinued, now that the supply of pure penicillin is plentiful.

2. *Research.*—Since the introduction of sulphonamide therapy, few specimens of sputum have been sent for examination in pneumonia cases. A study of seven lungs from patients who had died of pneumonia in spite of sulphonamide treatment showed drug-resistant strains of pneumococcus in them, Friedlander bacillus in two, and *Staphylococcus aureus* and *H. influenzae* in another. A serum prepared from highly virulent strains of *H. influenzae* isolated from cases of meningitis, was found very effective in influenzal meningitis when used with sulphathiazole. The immunizing effects of typhoid endotoxoid were studied in a gold mine; it has virtually eradicated the disease. Immunization with a virulent vaccine against plague has been widely practised in threatened areas with good results; it gave a high degree of protection, though the vaccinal reaction was mild in nature. Large numbers of cases of relapsing fever were studied, their origin traced and recommendations made with a view to the prevention of spread. An investigation was carried out on the epidemiology of typhus in the Transkei. A louse 'census' is being taken and may shed light on seasonal variations in their density and other important questions; the cropped hairs of prisoners collected and boiled in a solution which dissolves the hair but leaves

the lice intact, so that they can be counted. Studies of the serological tests for the diagnosis of typhus fever with rickettsial agglutination are being continued, and a paper has been prepared for publication; it is now possible in many cases to distinguish between louse typhus, flea typhus and tick typhus through these tests. A 'field' test has also been devised and enables a doctor to confirm his clinical diagnosis within a few minutes. There has been a considerable increase in the issue of skin test outfits and protein extracts for use in the diagnosis and treatment of allergic conditions. Various investigations on nutrition are proceeding.

THE FIFTEENTH ANNUAL REPORT OF THE ASSOCIATION FOR THE PREVENTION OF BLINDNESS, BENGAL, FOR THE YEAR ENDING 31ST MARCH, 1945

A CENSUS taken during the year in various parts of the province showed 294 persons blind out of a total of 182,176, i.e. 161.3 per 100,000. From the report it appears that the causes are manifold. Quacks and couchers still flourish and were responsible for several cases of absolute blindness. Ignorance and superstitious belief in the talisman and herbal remedies were found to be factors in many cases of unnecessary loss of vision. Other causes were venereal diseases, malnutrition leading to keratomalacia, smallpox, corneal ulcers following conjunctivitis, trachoma, cataract and glaucoma. And behind all this, of course, were poverty, apathy and lack of facilities for proper treatment.

The five dispensaries under the Association worked in ten districts, treating 54,954 cases and carrying propaganda on the prevention of eye diseases. Nearly one-third of the 1,674 operations were for extraction of lens. In addition, the eye examination and lecture unit in Calcutta examined 3,350 students and found defects in 1,020 (30.4 per cent), of which 711 (about 24 per cent of the whole) were due to errors of refraction. It would be interesting to know why these errors are so common in the town boys and girls.

Lieutenant-Colonel E. O'G. Kirwan, I.M.S., who was Honorary Secretary of the Association since its foundation, has retired. It owes much to him for its success. The Association is doing valuable work and could do more if greater financial support were forthcoming.

Correspondence

TREATMENT OF CARBUNCLE WITH PENICILLIN

SIR,—Among general diseases in the treatment of which penicillin has proved valuable, carbuncle is one. A British soldier in this hospital developed a carbuncle on the nape of the neck. Treatment on conservative lines with magnesium sulphate, glycerine and insulin had no curative effect, and the condition grew gradually so bad that operation seemed to be the only remedy. Accordingly the surgeon was sent for, but after a consultation, the patient was put on penicillin 20,000 units immediately and 15,000 units three-hourly and the carbuncle was strapped. After 24 hours, improvement became apparent in that the headache, pain and insomnia which had to be controlled with opiates eased; after 48 hours the surrounding inflammation and redness subsided, and after 96 hours the carbuncle dried up. When the last dose of penicillin was given on the sixth day, all that remained of the carbuncle were only a few healing holes.

P. V. KARAMCHANDANI, M.B., F.R.C.P.,
LIEUTENANT-COLONEL, I.M.S.,
O.C., C.M.H., and Medical Specialist,
Mehgaon (C. P.).

Service Notes

APPOINTMENTS AND TRANSFERS

LIEUTENANT-COLONEL S. SMYTH, Civil Surgeon, Simla East, is appointed to act until further orders as Civil Surgeon, Simla West, in addition to his own duties, with effect from the afternoon of the 8th September, 1945, *vice* Lieutenant-Colonel F. H. Whyte, granted leave.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

To be Captain

Maurice Ernest Winters. Dated 6th July, 1944.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

To be Captains

(Miss) Chittur Subramanya Ananthalakshmy. Dated 15th May, 1945.

S. R. Kulkarni. Dated 20th April, 1945.

P. M. Desai. Dated 13th July, 1945.

D. D. Singhi. Dated 14th July, 1945.

M. A. Durrani. Dated 27th July, 1945.

To be Lieutenants

(Miss) Nellyat Kunanakandy Sunanna. Dated 20th May, 1945.

M. P. Mathur. Dated 11th June, 1945.

D. S. Rastogi. Dated 15th June, 1945.

B. R. Baliga. Dated 13th July, 1945.

14th July, 1945

R. N. Sharma.

T. Fonseca.

M. S. N. Rao. Dated 16th July, 1945.

17th July, 1945

Shams-ur-Rahman.

K. Mustafa.

A. Rashid.

A. B. Awan.

A. Rashid. Dated 18th July, 1945.

19th July, 1945

M. Amin.

L. D. Khurana.

K. Ahmad.

R. Singh.

P. N. Trikha.

20th July, 1945

Syed Lamaat Ahmed Bokhari. Mujeeb-ur-Rahman.
Felix D'Souza. Dated 21st July, 1945.

The following officers are retransferred to the Army :—

ROYAL INDIAN NAVAL VOLUNTEER RESERVE

Ty. Surg. Lieut. Cdr. B. P. Srivastava. Dated 1st April, 1945.

Ty. Ag. Surg. Comdr. P. S. Clarke. Dated 17th May, 1945.

Ty. Comdr. (Sp.) M. H. A. Campbell, M.B.E. Dated 20th June, 1945.

Ty. Lieut. M. Maithland. Dated 23rd June, 1945.

Ty. Lieut. (Sp.) F. G. Wilson. Dated 13th July, 1945.

LEAVE

Lieutenant-Colonel F. H. Whyte, Civil Surgeon, Simla West, is granted 6 months' leave, on medical grounds *ex-India*, with effect from the 10th September, 1945, with permission to prefix Sunday, the 9th September, 1945, to his leave.

PROMOTIONS

Colonel to be Major-General

W. E. R. Dimond, C.I.E., C.B.E., V.H.S. Dated 23rd August, 1945.

Majors to be Lieutenant-Colonels

S. Annaswami. Dated 10th August, 1945.

de L. Carey. Dated 15th September, 1945.

Captain to be Major.

J. H. Caverhill. Dated 28th August, 1945.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Captains to be Majors

J. R. Davison. Dated 3rd August, 1945.

6th August, 1945

A. B. Gilroy. B. A. Lamerell.

R. Nagendran. Dated 15th July, 1945.

1st August, 1945

R. S. Dhillon. R. K. Satija.

M. Das Gupta.

2nd August, 1945

K. C. Choudhuri. S. M. Das.

S. C. Banerjee. C. K. P. Menon.

C. K. P. Rao. Dated 3rd August, 1945.

R. Viswanathan. Dated 4th August, 1945.

V. P. Rao. Dated 5th August, 1945.

15th August, 1945

P. Singh. C. B. Chaudhery.

N. L. Sharma. I. A. Sahibzada.

B. L. Aggarwal. J. Sen.

L. M. Ram. Dated 21st August, 1945.

C. R. Mannadiar. Dated 26th August, 1945.

INDIAN MEDICAL SERVICE

SECONDED TO THE ROYAL INDIAN NAVY

(Emergency Commissions)

Lieutenants to be Captains

S. G. Ramaiya. Dated 7th August, 1945.

J. T. Marshall. Dated 27th August, 1945.

K. Kumar. Dated 28th August, 1945.

E. A. Corbett. Dated 29th August, 1945.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Lieutenants to be Captains

B. S. Kulkarni. Dated 5th April, 1945.

(Mrs.) J. L. Khan. Dated 14th May, 1945.

J. S. Puri. Dated 10th July, 1945.

G. B. Singh. Dated 2nd August, 1945.

6th August, 1945

T. K. Jayram. C. Visakam.

A. K. Nilkantan. V. K. Visvanathan.

K. Karunakaran. Dated 7th August, 1945.

8th August, 1945

S. Venkataraman. P. T. B. Varma.

N. Narayanasamy. G. A. S. Krishnamurti.

V. Ramchandran. K. D. N. Karan.

9th August, 1945

M. G. Varadarajan. M. Ubeidullah.

M. A. Gokhale. G. Venkatappan.

H. S. Anand.

24th August, 1945

B. E. G. Garson. A. M. Jafar.

H. D. Singh. Dated 25th August, 1945.

Ata-ul-Haq Chaudhuri. Dated 26th August, 1945.

27th August, 1945

P. J. Kennedy. D. E. Jeremiah.

29th August, 1945

M. B. Sopher. D. N. Bhowmik.

A. K. Mitra. M. A. Majid.

B. N. Ghose. Dated 31st August, 1945.

(WOMEN'S BRANCH)

Lieutenants to be Captains

Miss L. M. B. Copland. Dated 25th July, 1945.

Miss S. J. Mistry. Dated 19th August, 1945.

RETIREMENTS

Lieutenant-Colonel Byram Sorabji Dhondy. Dated 27th July, 1944.

Colonel A. C. Macrae, V.H.S., I.M.S. Dated 29th October, 1944.

RELINQUISHMENTS

The undermentioned officers are permitted to relinquish their commissions on grounds of ill health and are granted the honorary rank of Majors:—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE

SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Captain (Miss) S. M. Terway and Captain S. G. A. Raju, 21st September, 1945, on grounds of ill health, and are granted the honorary rank of Captain.

Major R. Rajagopalan. Dated 2nd October, 1945.

RESIGNATIONS

The undermentioned officers are permitted to resign their commissions subject to His Majesty's approval and are granted the honorary rank of Captains:—

INDIAN MEDICAL SERVICE

SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Captain (Mrs.) S. M. L. Howell Roberts. Dated 26th June, 1945.

Captain (Mrs.) L. C. Hylton (Neé Paterson). Dated 26th June, 1945.

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